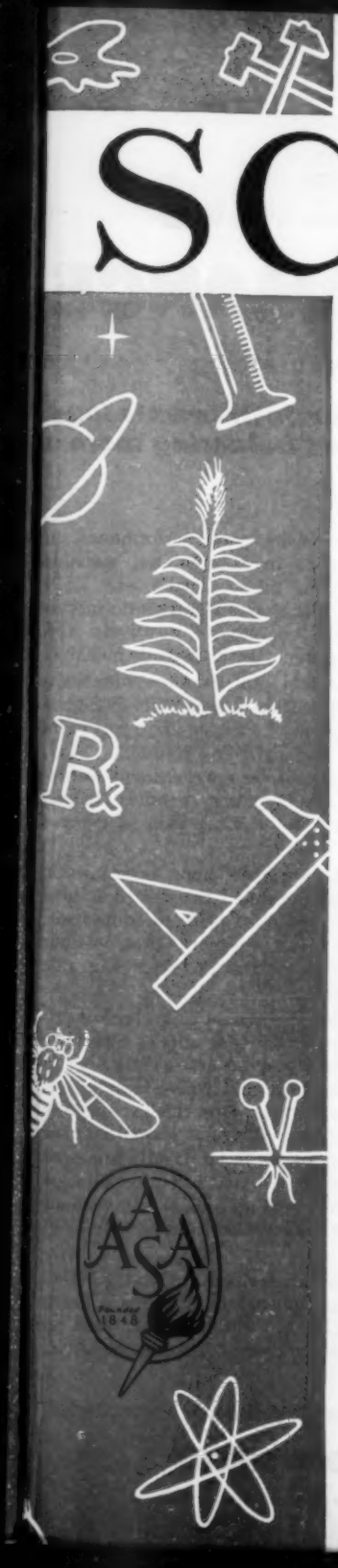

SCIENCE

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AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

1. Center line of slidewire and shaft
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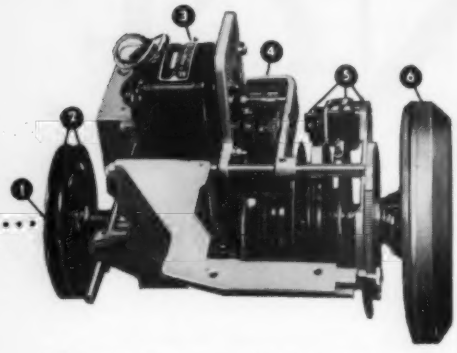
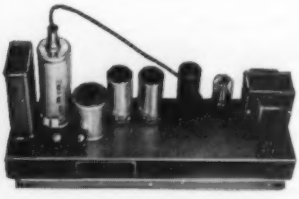
3. Balancing motor
4. Spring-loaded no-backlash drive
5. Control slidewires
6. Measuring slidewire



This partially dis-assembled view of Speedomax shows its two-phase Balancing Motor and gears, with a typically "heavy" load of slidewires and contacting cams for signal and control devices. Several more cams, etc., can be added if necessary; only practical limit is physical space on shaft. Smoothness in operating many contacts is an outstanding Speedomax ability.



Amplifier which feeds the Speedomax balancing motor the controlling half of its power. Torque gradient is especially high where needed most—around balance point—for prompt, positive balancing. This Amplifier leads its field by large margins in sensitivity and in power output.

Good circuit engineering shows in this Slidewire's non-inductive wiring and in the absence of any flexible leads which might form inductive loops.

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Ion-Scattering Analyzer

STANFORD RESEARCH INSTITUTE has a new instrument capable of identifying and measuring minute quantities of the elements present in the surface of a material—the ion-scattering analyzer. This "proton bombarder" consists of a two-million volt generator, a twenty-foot vacuum tube, and two large electromagnets. It weighs about five tons, yet it can detect as little as 1^{-12} gram. The device bounces protons off the atoms composing the surface of a sample into a spectrometer that sorts them according to their rebound velocities (just as an optical spectrometer sorts light waves according to their wavelengths) and feeds them into a counting device. Since the velocity of the protons depends upon the weights of the atoms that deflect them, the various velocities coming from a bombarded surface indicate which elements are present. The relative numbers of protons reveal the proportional composition of the surface.

A van de Graaf type generator delivers the high voltage needed in the apparatus, and a vacuum tube runs down its center to a large electromagnet. The high voltages produced are insulated, by nitrogen under pressure, from the heavy steel tank that contains the generator, and an endless belt carries charges up to be accumulated on a high-voltage electrode at the top. Hydrogen gas, leaking slowly from a small tank inside the electrode, is ionized in an arc discharge. The resultant ions are accelerated downward through the vacuum tube by the successive voltages of a series of hollow electrodes spaced along the interior of the tube. Emerging from the accelerator, the stream of ions is focused into a beam which contains protons, as well as the multiple hydrogen ions produced in the hydrogen ionization. The ions are separated from the protons, and the proton beam enters the target chamber, striking the small target area on the surface of the sample, where most of the protons are absorbed. Some of them come close enough to atomic nuclei to be bounced out again, losing energy to the atoms hit in inverse proportion to their atomic weights.

The protons that are allowed to pass through the spectrometer to the counting device are those with a definite, limited range of velocity. For maximum resolution of the various elements, the target area is narrowed down by regulating the entrance slits that shape the beam to a very small spot. The exit slit of the spectrometer is about the same size. Behind it is a thin layer of phosphorescent material on the end of a photomultiplier tube. Target chamber and tube are so arranged that a sharp "image" of the target area is focused on the phosphor, which emits light pulses when struck by protons. In contrast to an optical spectrometer, which scans over a focal plane, the magnetic spectrometer covers that part of the proton velocity range desired by varying the magnetic field in a series of "runs" to permit protons of different velocities to reach the counting circuit.

The number of protons that hit the target is kept the same for each of a series of runs by a current integrating circuit, and in each run a different fraction of the total is counted by the photomultiplier tube. Plotting the particular ratio setting used against the number of protons counted for each run gives a curve that looks like a series of steps, each of which corresponds to a different atomic mass in the sample, and the height of the step is proportional to the concentration.

The ion-scattering analyzer will be used initially to study surface modification of ferrous alloys, crystal boundary contamination of some nonferrous metals, and intermetallic diffusion, for the Ordnance Department of the Army. Stanford Research Institute also expects that many industrial applications will be found.

WILLIAM C. ESTLER

Stanford Research Institute
Stanford, California

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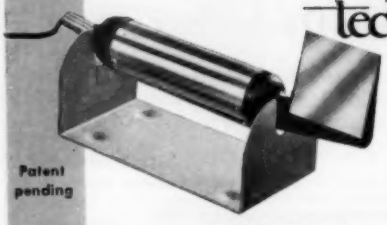

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Antispirochetal Interference between Antibiotics and Arsenoxide

N. Ercoli and G. M. Carminati

Istituto Sieroterapico Milanese Serafino Belfanti, Milano, Italy

IT HAS BEEN REPORTED RECENTLY that BAL (dimercaptopropanol) inhibits the antispirochetal effect of penicillin, bacitracin, and chloromycetin as it does that of the metal-containing (As, Au) compounds, whereas streptomycin, aureomycin, terramycin, and subtilin are not inhibited by the dithiol. This BAL reversal of antiprotozoan action is a specific one, inasmuch as the antibacterial action is conserved and seems to be related to the chemoreceptor mechanism (*1*). Exploring further the mechanism of antispirochetal action, we have studied the effect of combined treatment with known antiprotozoan agents.

Therapeutic experiments were carried out on mice infected (20 hours before) with an African strain of *Borrelia duttoni*,[1] against which the effective (subcutaneous) doses[2] for each drug investigated had been accurately determined (*2*). Characteristic details of the combination experiments appear in Tables 1–3. It was found that the antispirochetal activity of arsenoxide was additively or synergistically enhanced by combined treatment with the antibiotics streptomycin, penicillin, or bacitracin: the same result was obtained with arsenoxide and myochrysin. In contrast, simultaneous treatment with arsenoxide and the antibiotics terramycin, aureomycin, or chloromycetin both decreased the immediate action of the antibiotic and the delayed one of arsenoxide. This phenomenon of interference with arsenoxide activity appeared with effective, as well as ineffective, doses of the antibiotics. For example, 1.5 mg/kg terramycin—a dose that does not inhibit the rapid increase of the spirochetes—interfered noticeably with the effect of 5 mg/kg arsenoxide (which, given by itself, clears the blood stream of parasites within 24 hours). On the other hand, the interference effect disappeared if the dose of either arsenoxide or the antibiotic was increased sufficiently above the therapeutic range. Effective doses (5–10 mg/kg) of arsenoxide, for example, inhibited the immediate effect (3–5 hours) of 4 mg/kg terramycin, but not that of 8 mg/kg. Conversely, 2–4 mg/kg terramycin or aureomycin inhibited the delayed action (22–45 hours) of 5 mg/kg arsenoxide, but not that of 10–20 mg/kg. It should be mentioned that, as a result of interference with the early action of the antibiotic, the *immediate* antispirochetal effect of the latter combinations was lower than that corresponding to antibiotic treatment alone.

TABLE 1

THERAPEUTIC INTERFERENCE BETWEEN TERRAMYCIN AND ARSENOXIDE IN THE *Borrelia duttoni* INFECTION OF MICE
(Expt No. 110)

Treatment	No. spirochetes in 25 dark fields (Hours after treatment)				
	0	3	5	22	44
None	37	120	200	500	1000
	50	125	200	450	900
	25	120	225	550	750
Arsenoxide, 5 mg/kg	50	75	25	0	0
	40	40	10	0	0
	25	65	12	0	0
Aureomycin, 4 mg/kg	35	8	1	0	0
	50	4	0	0	0
	40	6	0	0	0
	25	0	0	0	0
Arsenoxide, 5 mg/kg + aureomycin, 4 mg/kg	40	50	85	4	3
	40	40	75	80	1
	50	40	75	10	0
Arsenoxide, 10 mg/kg + aureomycin, 4 mg/kg	40	40	50	0	0
	40	25	40	0	0
	35	20	12	0	0
	25	20	10	0	0
	35	22	20	0	0
Arsenoxide, 20 mg/kg + aureomycin, 4 mg/kg	40	12	4	0	0
	40	1	2	0	0
	40	15	2	0	0
	35	25	1	0	0
	50	20	35	0	0

Chloromycetin, aureomycin, and terramycin, characterized by a similar wide antibiotic spectrum, interfere with the antispirochetal action of arsenoxide. The similarity of these antibiotics as antibacterial, antiprotozoan, and antirickettsial agents, and as producers of cross-resistant strains (*3–5*), finds analogy in their common ability to interfere with the antispirochetal activity of arsenoxide. From the majority of the re-

[1] Strain received in 1949 from the Pasteur Institute, Paris.

[2] The minimal *clearing* and *reducing* doses—i.e., the doses giving total disappearance, respectively 80–95% reduction of the circulating spirochetes, within 3–5 hours—have been determined for the subcutaneous method of administration. The reduction of the spirochetemic curve appears with greater delay, but it is more persistent in the case of arsenoxide and streptomycin than in that of the other antibiotics. Arsenoxide doses of 2.5–5.0 mg/kg give 80–95% reduction in less than 22 (and more than 6) hours; to obtain clearing within 5–6 hours, arsenoxide doses of 20 mg/kg are required. The drop in the spirochete count appears more promptly, although with a greater tendency to rise again, with the other antibiotics. The subcutaneous reducing doses were the following: terramycin, aureomycin, 2–4 mg/kg; bacitracin, 7 mg/kg; subtilin, 8 mg/kg; penicillin, 8–10 mg/kg; chloromycetin, 35 mg/kg; streptomycin, 75 mg/kg. The clearing doses were 50–100% higher.

TABLE 2

THERAPEUTIC INTERFERENCE BETWEEN TERRAMYCIN AND ARSENOXIDE IN THE *Borrelia duttoni* INFECTION OF MICE

Treatment	No. spirochetes in 25 dark fields (Hours after treatment)				
	0	3	5	22	44
Expt No. 108					
Terramycin, 4 mg/kg	25	3	3	20	380
	35	10	7	50	500
	35	18	10	35	500
Arsenoxide, 5 mg/kg	35	35	20	0	0
	50	50	22	0	0
	35	75	15	0	0
Terramycin, 4 mg/kg + arsenoxide, 5 mg/kg	35	25	20	18	1
	35	35	18	6	0
	35	35	70	20	25
Expt No. 131					
Terramycin, 1.5 mg/kg	25	75	60		8
	25	75	125		12
Terramycin, 3 mg/kg	50	2		0	3
	25	4		0	0
Arsenoxide, 5 mg/kg	25	80		0	0
	35	80		0	0
	50	60		1	0
Terramycin, 1.5 mg/kg + arsenoxide, 5 mg/kg	25	60		15	0
	60	75		3	25
	35	50		5	5

ports (*5–10*) it would seem that they also share the ability to interfere with the antibacterial action of penicillin and streptomycin.

Of the three antibiotics interfering with arsenoxide, only chloromycetin is inhibited, as are penicillin, bacitricin, and arsenoxide itself, by BAL in regard to its antispirochetal effectiveness. On the basis of the assumption that BAL-reversibility is related to the action on chemoreceptors (*1*), it can be concluded that the antibiotic interference with arsenoxide is not bound to this action.

In all our experiments the interference phenomenon appeared as a decrease of activity of both drugs used for combined treatment (antibiotic and arsenoxide). The phenomenon is mostly manifest at *minimal effective dose* ranges (or even below) and resembles a decrease of dosage in all its manifestations (reduction of the parasite count, relapses).

To interpret these findings, we arrived at the following working hypothesis, which seems to agree with the known facts and the present observations. *Therapeutic interference* is the result of a reciprocal competition between effective drugs in an *elective* process of fixation-penetration on or in the microorganism. This competition—which presumes a similar elective mechanism of fixation-penetration—reduces the concentration of the competing drugs below the levels required to affect the receptors to the point of measurable therapeutic response. The competition in the process of fixation-penetration can take place between drugs acting on identical or on different receptors—i.e., through the same or through a different type of biochemical lesion.

1) The strongest supporting evidence for this thesis lies in Jancsó's experiments: pretreatment with pararosaniline protects trypanosomes against lethal photosensitization to acriflavine, as a result of decreased fixation of the latter drug (*11*). Earlier, Hirschfelder and Wright (*12*) attributed to "a simple surface reaction" the antagonism between acriflavine and triphenylmethane dyes on the inhibition of CO_2 production by yeast cells. This effect was obtained by staining the cells with ineffective methyl violet or brilliant green doses and exposing them to acriflavine, or vice versa, after exposing them first to ineffective acriflavine concentrations and then to the other dye. In our opinion, other evidence can be seen in the "separated interference" experiments of Schnitzer (*13*): trypanosomes treated with pararosaniline in one host, after passage to another (mouse), were not affected by therapeutic acriflavine doses.

2) The existence of an optimal dose for interfering effect established in 1927 (*14*) for pararosaniline/acriflavine and pararosaniline/arsphenamine, since confirmed in a number of other cases, shows that the competition can be overcome by an excess of one of the therapeutic agents. In the examples presented above, the immediate effect of the antibiotic, as well as the delayed action of the arsenical, was re-established by

TABLE 3

THERAPEUTIC INTERFERENCE BETWEEN CHLOROMYCETIN AND ARSENOXIDE IN THE *Borrelia duttoni* INFECTION OF MICE
(Expts 107 and 108)

Treatment	No. spirochetes in 25 dark fields (Hours after treatment)				
	0	3	5	22	44
Chloromycetin, 15 mg/kg	50	35	75	350	+++
	50	50	40	40	+++
	25	40	40	500	+++
Chloromycetin, 60 mg/kg	40	0	0	0	0
	25	0	0	0	0
	25	1	0	0	0
Arsenoxide, 5 mg/kg	50	50	22	0	0
	35	50	20	0	0
	35	60	20	0	0
Arsenoxide, 10 mg/kg	35	25	10	0	0
	50	35	6	0	0
	35	35	6	0	0
Chloromycetin, 15 mg/kg + arsenoxide, 5 mg/kg	25	35	20	2	15
	35	25	22	20	20
	25	25	25	12	25
Chloromycetin, 60 mg/kg + arsenoxide, 5 mg/kg	25	5	5	2	35
	35	12	8	4	50
	25	10	6	3	35
Chloromycetin, 60 mg/kg + arsenoxide, 10 mg/kg	35	5	3	2	2
	35	6	8	4	0*
	25	10	5	1	1

* Relapsed within 24 hr.

increasing the dosage of one or the other drug. These observations prove that the receptors of the cell did not lose their sensitivity to the therapeutic action of the interfering drugs; provided the drug arrives in sufficient quantity a therapeutic effect will take place.

3) Fractions of the minimal dose of terramycin, aureomycin, and chloromycetin are sufficient to interfere with the therapeutic effectiveness of arsenoxide. This is another fact confirming the view that interference is independent of a cellular lesion (and of the receptors). Therapeutically ineffective doses of one drug are sufficient to compete with the cellular fixation mechanism of the other drug to an extent that reduces its uptake below effective levels.

4) The possibility that chemoreceptors influence this phenomenon is minimized or excluded by other facts which demonstrate that the interfering effect is independent of therapeutic action. The fundamental observation that led to interference studies was made with an inactive drug. Morgenroth and Rosenthal (*15*) reported in 1911 that the trypanocidal activity of antimonyltartrate was inhibited by hexatantalate, an ineffective compound that could, nevertheless, induce drug resistance to antimonials. The inhibiting effect of the inactive hexatantalate was obtained later for certain arsenicals (e.g., arsphenamine), but not for others (arsenoxide) (*16*). Interference between two *active* drugs was observed first by Browning and Gulbransen in 1922 (*17*) with pararosaniline/acriflavine and a trypanosome strain that was resistant to pararosaniline itself. Pararosaniline-resistant strains showed the same interference phenomenon with pararosaniline/arsphenamine and pararosaniline/arsecatine (*16, 18*) as did normal strains. Thus the sensitivity of the microorganism to the therapeutic effect of the drug is not a determining factor in the interference phenomenon. In fact, Hasskó (*19*) quantitatively demonstrated that certain therapeutically ineffective triphenylmethane dyes decrease the fixation of acriflavine in the trypanosomes.

In relation to these observations we investigated whether penicillin, aureomycin, terramycin, and chloromycetin—which are inactive in the *Trypanosoma equiperdum* infection of mice—have any influence on the trypanocidal activity of arsenoxide. No measurable effect was found. We also established that chloromycetin, aureomycin, and terramycin do not influence the host toxicity of arsenoxide.

5) The characteristic time/effect curves of the interfering drugs in our study permitted the demonstration of the *reciprocal* nature of the interference between active drugs. This reciprocal effect is most suggestive of a competitive mechanism. It is difficult, in general, to attribute therapeutic effect to one or the other of the interfering drugs. We are, however, under the impression that the reciprocity of the interference is much more frequent than has been demonstrable so far; and, consequently, we consider that the positions of the "interfering" and the "interfered" drugs may be only relative, depending on the particular conditions of the experiment.

6) The possibility that the competitive process takes place at the level of the receptors (i.e., that it should be biochemical in nature) rather than in the fixation process is considered unlikely—a view substantiated not only by the facts outlined but by logic. (*a*) If two active drugs are acting on the same sensitive receptors (i.e., by identical biochemical lesion), it is not conceivable that the displacement of one active drug by another should result in a lower therapeutic effect, except in the case of extreme quantitative differences of activity, which in the examples studied do not occur. (*b*) If the two drugs are acting on different receptors, the effect of the lesions determined by one drug could not influence those attributable to the other in any way except synergistically. An interesting example is the interference described for arsenoxide and aureomycin (or terramycin), in view of the fact that, in accordance with their dithiol reactivity, these drugs are assumed to have different receptors.

7) We assume that the underlying cause for competitive fixation is an analogous absorption-fixation pattern of the interfering drugs. Hypothetically this might depend on a similar mechanism of cellular uptake (e.g., analogous binding forces), or on the fixation of the two drugs by the same specialized zones of the cellular surface. It would be difficult to imagine the number of possibilities which a polyphase structure such as that of the protoplasm might possess as far as mechanisms of fixations are concerned, considering that even the surface of homogeneous materials presents differentiated patches of adsorptive power in relation to various substances (*20*). Quastel and Wooldridge (*21*), studying the effect of various chemicals on resting *Bacillus coli*, a quarter of a century ago, expressed the view that the cell surface is composed of active centers "made up of a number of groupings each of which plays its part in determining the access of a substrate to the centre."

Without the concept of a differentiated and elective cellular absorption (fixation-penetration), it would be extremely difficult to explain why interference does not occur each time two active drugs, each of which is no doubt becoming bound to the microorganism, are used.

Possibly it is in relation to an analogous mechanism of uptake that the three antibiotics which interfere with arsenoxide (and possess similar spectra) are the same antibiotics which exert—like arsenoxide itself—a high *in vitro* action against the spirochetes (*2*).

Therapeutic interference (which is the name given to the phenomenon by Browning and Gulbransen) can take place between an antibiotic and a totally different type of compound (arsenoxide), as well as between two antibiotics (*6–10*). Also, in bacterial infection, we can cite a case of interference between an antibiotic and a metallic compound: gold-sodium-thiomalate interferes with the therapeutic activity of subtilin in the hemolytic streptococcus infection of mice, as noted by one of us in collaboration with B. S. Schwartz in 1949 (*22*).

These findings seem to indicate that antibiotics pos-

sess the same aptitude as other drugs to enter into antagonistic pairs. No doubt the "antibiotic antagonism" is only a particular example in the broader field of the therapeutic interference, and it could be examined in this light. It is claimed (*23*) that the interference of chloromycetin with the antibacterial action of penicillin is related to the bactericidal function of the latter antibiotic, since interference appeared only in this early phase of action; further, that the bactericidal action of penicillin is not exerted on the microorganism in a state of bacteriostasis determined by the interfering antibiotics (*9*). In view of the fact that in all cases of interference there is an optimal time element—as established first in 1911 (*15*)—which may be related to the time period required for fixation, it remains questionable whether the conditions described as the cause of the interference between two antibiotics are not rather incidental.

We realize, of course, that the assumption of a differentiated process of fixation does not simplify the question of the mechanism of antiprotozoan action; in fact, for its understanding, new questions have to be answered (the mode and factors responsible for it, grouping of drugs from standpoint of fixation, etc.). No single mechanism of action is conceivable, however, that could account for the complex and highly specific manifestations of antiprotozoan action, such as the selective action of chemically similar drugs, or the different dispersion of antimicrobial spectra. These could be better understood as being linked to a number of superimposed mechanisms which may vary to different extents from one to another drug/microorganism system.

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News and Notes

Centennial Convention, A.Ph.A.

More than 1500 pharmacists from all parts of the world converged on Philadelphia Aug. 17–22 for the 1952 convention of the American Pharmaceutical Association, which was observing its 100th anniversary. The association was founded in 1852 by 24 progressive pharmacists; today, a hundred years later, it lists a membership of over 25,000, from all branches of pharmacy.

The convention officially opened Aug. 17 with an address by Clarence E. Pickett, honorary secretary of the American Friends Service Committee. A symphony concert by 45 musicians, recruited largely from the Philadelphia Orchestra, was a part of the opening exercises. The concert was under the direction of Norman Black. Hugh C. Muldoon, dean of the College of Pharmacy, Duquesne University, Pittsburgh, and chairman of the Committee on the Centennial Celebration, presided at this program, and Don E. Francke, president of the A.Ph.A., gave a short address of welcome before Dr. Pickett spoke.

In his address Dr. Pickett urged Americans to have increased interest in the peoples of other nations, and to accept the humanitarian responsibilities forced upon America as the leading world power. He further stated that if people at large would apply the same integrity to their lives and their understanding of world conditions as the pharmacist and the scientist apply in their everyday work, the world would be far better for all.

The business sessions of the convention began on Aug. 18 with the first meeting of the House of Delegates and the first general session. The House which, as the association's governing body, is made up of delegates from all branches of pharmacy, including teaching, manufacturing, wholesaling, retailing, law enforcement, and research, heard committee reports, named committees, and considered organizational plans. At the first general session, welcoming addresses by the local committee were followed by a tribute to the past presidents of the association by Robert L. Swain, editor of *Drug Topics*, and a past president of the A.Ph.A., who spoke on "The A.Ph.A.

Presidency—a Symbol of Duty and Obligation." Sixteen of the 19 living past presidents were present, and each received a special citation and a lapel pin in testimony of his untiring efforts in behalf of the association's growth. Following the presentation of the citations, Dr. Swain then presented one to President Francke, who was to retire later in the week when the president-elect was inaugurated.

Dr. Francke delivered his presidential address at this meeting, reviewing the hundred-year history of the association and noting areas for future development. Singling out the need for more local branches, to bring the activities of the association closer to the rank and file of the membership, Dr. Francke urged the creation of more branches to serve as centers for the professional life of pharmacists, and to foster the professional development of young college graduates.

At the second general session, W. J. Tristram, president of the Pharmaceutical Society of Great Britain, reviewed the results of the National Health Service program in Great Britain. Emphasizing that he was not urging adoption of a similar plan for the United States, he nevertheless pointed out that Britain's social program resulted in early diagnosis of physical ills and more immediate treatment, which undoubtedly had had some effect on the life span of the British people. Mr. Tristram was followed by Louis H. Bauer, president of the American Medical Association and secretary-general of the World Medical Association. Dr. Bauer provided the 1000 members of the A.Ph.A. in attendance at the session with the first official description of the work of the World Medical Association that they had yet heard. Reporting on the surveys of health conditions in foreign countries, Dr. Bauer noted that this was but one of the many achievements of the organization in its brief existence. He, too, called upon the pharmacists to pay more attention to the problems of health throughout the world in the years to come.

President-elect Richard Q. Richards, of Fort Myers, Fla., who was installed on Thursday at the close of the convention, in his inaugural address called upon representatives of the American Medical Association, the American Dental Association, and the American Nurses Association to meet with representatives of the A.Ph.A. to formulate an "Interprofessional Code of Ethics" that would outline the relations between and among these health professions. "If such a code is promulgated," Mr. Richards maintained, "many of the interprofessional problems now facing us would be solved automatically."

High light of the week's convention was Wednesday, when the centennial of the American Pharmaceutical Association was observed in dramatic afternoon ceremonies in the Bellevue-Stratford Hotel, and at a banquet held in Philadelphia's Municipal Auditorium. Both programs were witnessed by more than 1500 people.

At the afternoon ceremony, representatives of 25 foreign pharmaceutical and scientific societies presented greetings to the A.Ph.A. on its centennial, and representatives of 86 domestic societies joined in the academic procession to present their greetings as well. A letter from President Truman, paying tribute to the Association's work over the past hundred years, was read by Dr. Francke, who also presided at the ceremonial session.

Following the academic procession, the invocation was delivered by Elof F. Johnson, curate of the Church of the Redeemer, Bryn Mawr, Pa., himself a former pharmacist. W. R. Cutler, president of the Pharmaceutical Association of Australia and New Zealand spoke in behalf of all the foreign organizations present in a tribute to the A.Ph.A., and George H. Beal, chairman of the council of the association, and director of research at the Mellon Institute, responded to Mr. Cutler's greetings. Malcolm T. MacEachern, director of professional relations of the American Hospital Association, spoke for the domestic organizations, and Leonard Scheele, surgeon general of the U. S. Public Health Service, brought the greetings of government agencies to the association. Robert P. Fischelis, secretary of the A.Ph.A., responded, and following the presentation of scrolls Ivor Griffth, president of the Philadelphia College of Pharmacy and Science, delivered the major address on "Values that Endure in the Practice of Pharmacy." It was in Dr. Griffth's college that the American Pharmaceutical Association was formed in 1852, and Daniel B. Smith, its first president, was also president of the college at that time.

At the banquet, Hugh N. Linstead, a member of the British Parliament and secretary of the Pharmaceutical Society of Great Britain, delivered the major address and called upon members of the American Pharmaceutical Association to take a more active part in the affairs of the International Pharmaceutical Federation. Noting that the members of the A.Ph.A. had attended many of the meetings of the international group, Mr. Linstead also urged that an American committee be appointed to work with the international organization, in an effort to disseminate the work of both organizations more widely.

In addition to the general sessions, meetings of the sections of the association were also held. The Scientific Section heard 120 papers covering a wide range of subjects, and most of the papers presented will appear in subsequent issues of the Scientific Edition of the *Journal of the American Pharmaceutical Association*. Papers read before the sections on Education and Legislation, Practical Pharmacy, Economics, and History will be published in subsequent issues of the Practical Pharmacy Edition of the *Journal*.

Officers installed at the final general session on Thursday morning were: Richard Q. Richards, president; Tom D. Rowe, dean of the University of Michigan College of Pharmacy, first vice president; and Charles Lanwermeyer, chief pharmacist, Abbott Laboratories, second vice president. New members of the council are Henry H. Gregg, of Minneapolis; George Moulton, of Peterborough, N. H.; and Walter M. Chase, of Parke, Davis & Co. Robert P. Fischelis and

Hugo H. Schaefer, dean of the Brooklyn College of Pharmacy, continue in office as secretary and treasurer, respectively.

Nominees for president-elect, to be voted on by mail ballot, are Newell Stewart, secretary of the Arizona Pharmaceutical Association; F. Royce Franzoni, practicing pharmacist of Washington, D. C., and former president of the National Association of Boards of Pharmacy; and LeRoy Weidle, practicing pharmacist of St. Louis, Mo.

Scientists in the News

Melvin R. Arnold, formerly with the Girdler Corporation, has joined the research staff of the Miner Laboratories. He will serve as assistant to C. S. Miner, Jr.

Robert C. Cook, editor of the *Journal of Heredity* and director of the Population Reference Bureau, Inc., is attending the World Conference on Planned Parenthood in Bombay. The conference is sponsored by the Family Planning Association of India. Flying around the world, Mr. Cook will visit many population trouble spots on his journey.

William C. Coombs has been named to the staff of the Denver University Institute of Industrial Research. He will serve as a project supervisor with the institute. Mr. Coombs was formerly connected with the Southwest Research Institute, San Antonio.

Kenneth Willard Cooper, associate professor of biology at Princeton University, has been appointed professor of biology and chairman of the Department of Biology at the University of Rochester. He will succeed **Donald R. Charles,** who has resigned as department chairman in order to devote more time to teaching and research. Dr. Charles will remain at the university.

Alastair Graham, professor and head of the Department of Zoology at Birkbeck College, University of London, and a recent recipient of the Keith Prize of the Royal Society of Edinburgh, has succeeded **Charles H. O'Donoghue** in the chair of zoology at the University of Reading.

Beno Gutenberg, professor of geophysics and director of the Seismological Laboratory at California Institute of Technology, has been awarded the Charles Legrange Prize by the Académie Royale de Belgique, Classe des Sciences, for his geophysical research. The prize is given every four years by the scientific division of the government-sponsored Belgian Academy for achievements in geophysics. Dr. Gutenberg is also serving a three-year term as president of the International Association of Seismology and Physics of the Earth's Interior.

The 1952 Thurman H. Bane Award, given annually by the Institute of Aeronautical Sciences in recognition of outstanding achievements in aeronautical development, was presented posthumously to **Patrick L. Kelly,** of the U. S. Air Force. Major Kelly's widow, Virginia O. Kelly, of Midland, Texas, received the award from Albert Boyd, commanding general of Wright Air Development Center. The institute also gave its 1952 Award to **Henry Seeler,** of Wright Air Development Center's Aeromedical Laboratory, for his development of a high-altitude respirator.

The staff of the Special Juvenile Delinquency Project of the Children's Bureau has been strengthened by the temporary addition of **Charles W. Leonard,** superintendent of the Illinois State Training School for Boys, and **Douglas MacNeil,** director of the Division of Community Services of the Department of Institutions and Agencies of New Jersey. Mr. Leonard will be with the project for three months to formulate and secure professional acceptance of a code of standards for training schools. During the two months he is to be with the project, Mr. MacNeil will devote himself to fact-finding and to the campaign for state and local action.

Donald P. Lessig, a graduate student in civil engineering at Carnegie Institute of Technology, has been named Rust Engineering fellow at Carnegie for 1952–53. The new fellowship provides a grant of $3300 for fundamental research work by a graduate student in civil engineering. Mr. Lessig's fellowship project is "Pressure Caused by Bulk Storage of Granular Materials."

Ernest Livingston has been appointed deputy chairman of the Chemistry Department, Brooklyn College, and **Robert Ginell** has been appointed deputy chairman of the Graduate Division of the Chemistry Department.

A. A. Miles, who has been director of the Division of Biological Standards at the United Kingdom's National Institute for Medical Research since 1946, and deputy director of the institute since 1947, has succeeded **Alan Drury** as director of the Lister Institute in London. Following his retirement from the institute after nine years of service, Sir Alan is now engaged in research in the Agricultural Research Council's Institute of Animal Physiology.

J. Cecil Mitcheson will succeed **R. J. Weeks** as president of the Institution of Mining Engineers of Great Britain for 1953–54. He will take office at the annual general meeting in January.

Cyril Leslie Oakley, who has been associated with the Wellcome Research Laboratories at Beckenham, England, since 1934—as head of the Immunology and Experimental Pathology Department since 1947—has been appointed to the Brotherton chair of bacteriology at the University of Leeds. He succeeds **James Walter McLeod,** who retired after 30 years of service.

John G. Pierce has been appointed assistant professor of physiological chemistry, School of Medicine, University of California Medical Center, Los Angeles,

with leave of absence, 1952–53, for an Arthritis and Rheumatism Foundation Fellowship, Cambridge University, England. He was formerly assistant professor of biochemistry, Cornell University Medical College.

Richard J. Plunkett has been appointed secretary of the newly established Committee on Mental Health of the American Medical Association. Dr. Plunkett has been a member of the AMA's editorial staff for the past five years. The committee, established in March 1952, was formed primarily to consider problems in psychiatry and mental health. **Leo H. Bartemeier,** Detroit, is chairman.

Hubert J. Schlafly, Jr., has been elected vice president in charge of engineering of TelePrompTer Corporation. Mr. Schlafly went to TelePrompTer from Twentieth Century-Fox Film Corporation, where he was director of television research. Prior to that he spent several years with General Electric at Schenectady, in its Electronics Laboratories.

P. A. Sheppard, university reader in meteorology in the Imperial College since 1939 and a former staff member of the Meteorological Office, has succeeded **David Brunt,** who retired from the chair of meteorology in the University of London and from the position of head of the Department of Meteorology, Imperial College of Science and Technology.

Louis M. Sherman has been appointed by Ethyl Corporation to the post of associate director of product development in charge of industrial chemicals. He will serve on the staff of William T. Hack, director of product development.

Leland B. Ticknor has been appointed instructor in chemistry at Swarthmore College. He has been on the research staff of the Division of Industrial Cooperation for the past two years.

Malcolm P. Tyor, a former associate in medicine at Bowman Gray School of Medicine, has joined the Medical Division of the Oak Ridge Institute of Nuclear Studies as a clinician. Dr. Tyor has been associated with the internal medicine group at Bowman Gray, which has carried out extensive research using radioisotopes as a tool in research and therapy.

Kasen Udyanin, head of the political science faculty at Chulalongkorn University, Bangkok, has been appointed visiting professor of government at New York University. Dean Udyanin has been a member of the Chulalongkorn faculty for 20 years and has served the Thai government as a provincial governor and ministry official. He has also been closely connected with the program of mutual security and a technical assistant in Thailand and Southeast Asia.

John C. Warner, president of the Carnegie Institute of Technology, **James B. Fish,** a former director of the AEC Division of Research and now director of physical research of the Bell Telephone Laboratories, and **Eugene P. Wigner,** professor of physics at Princeton University, have been named by President Truman to membership on the General Advisory Committee of the Atomic Energy Commission. The three succeed **J. Robert Oppenheimer, James B. Conant,** and **Lee J. DuBridge.**

Charles F. Wilkinson, Jr., professor and chairman of the Department of Medicine, New York University Post-Graduate Medical School, delivered the 36th Mellon Lecture before the Society for Biological Research of the School of Medicine, University of Pittsburgh. Dr. Wilkinson spoke on "Present Concepts of Atherosclerosis."

Education

Cornell University has established a Statistics Center to coordinate its consulting and teaching facilities in this field. Acting director will be Philip J. McCarthy, of the New York State School of Industrial and Labor Relations at Cornell.

The **University of Illinois** College of Medicine has appointed Erika Fromm clinical assistant professor in the Department of Otolaryngology, where she will direct the psychological aspects of the department's project on the diagnosis, psychotherapy, and educational handling of the brain-injured child. Louis Halperin has been appointed clinical assistant professor in the Department of Psychiatry.

The Department of Geology at **Massachusetts Institute of Technology** has been renamed the Department of Geology and Geophysics in recognition of the increased emphasis on instruction and research in geophysics. Two separate courses, one leading to a B.S. in geology and the other to a B.S. in geophysics, are now being offered. Both require the summer following the sophomore year to be spent at the MIT–Nova Scotia Centre for Geological Sciences at Antigonish. Following the junior year, students may participate in a cooperative seismic program with Geophysical Service, Inc., of Dallas.

Western Reserve University's School of Law will inaugurate a new graduate program in legal medicine, beginning in February. First course will be "Medical Aspects of Civil Litigation," and as the program expands, it will provide courses for lawyers, doctors, social workers, police prosecutors, and coroners.

At the **University of Wisconsin,** Aksel Lydersen, of the Technical Institute of Norway, Trondheim, is engaged in a study of American methods of education in chemical engineering. As a university project associate he is working with W. R. Marshall, Jr., on problems in vacuum drying and in design of spray equipment, and with O. A. Hougen on phases of applied chemical kinetics. Karl-Axel Melkerssen, of the Royal Technical Institute of Stockholm, is working under the direction of C. C. Watson on the fundamentals of separation processes. He holds a Swedish-American Foundation scholarship.

Grants and Fellowships

The **Commonwealth Scientific and Industrial Research Organization,** Melbourne, is offering studentships for postgraduate training both in Australia (15) and for training in the United Kingdom (9). Each will be for two years, and stipends will range from £A500 to £A600. Applications close on *Dec. 24.*

Three **Fellowships in Statistics** at the University of Chicago for 1953–54 are open to holders of the Ph.D. or its equivalent. The fellowships represent the third year of a five-year program supported by the Rockefeller Foundation to acquaint established research workers in the biological, physical, and social sciences with the crucial role of modern statistical analysis in planning experiments and in the study of empirical data. Closing date for applications is *Feb. 1,* and instructions for applying may be obtained from the university's Committee on Statistics, Chicago 37.

The **National Foundation for Infantile Paralysis** has available a limited number of postdoctoral fellowships in public health and preventive medicine. Stipends are based on individual need, but may cover tuition, maintenance, and an allowance for books. Candidates must be U. S. citizens, graduates of an approved school of medicine, and must have completed at least a one-year hospital internship. Also available is a limited number of postdoctoral clinical fellowships in physical medicine and rehabilitation. Eligibility requirements are the same, except that the age limit is 40. Full information may be obtained from the foundation's Division of Professional Education, 120 Broadway, New York 5.

RCA Fellowships, ranging from $1800 to $2700, have been awarded by Radio Corporation of America to the following graduate students: Oscar Oliver, Jr. (New York University); Hardy C. Martel (Caltech); Edgar Lipworth, of Salford, England (Columbia University); Mitchell S. Cohen (Cornell); Peter H. Lord (Princeton); and Edward W. Schwarz (University of Illinois).

Research Corporation has recently made grants totaling $120,000 to colleges, universities, and scientific institutions for specific research projects. Of the current grants, more than $85,000 is being distributed under the Cottrell grants program, named for the corporation's founder, to aid science and teaching in small colleges. The remainder will be used to support research primarily in the physical sciences.

Rockefeller Foundation grants for the third quarter of 1952, amounting to approximately $575,800, included a five-year grant of £25,000 to the University of Edinburgh Medical School; $26,000 to the American Museum of Natural History toward the costs of a restudy by Margaret Mead of a village community on Manus, one of the Admiralty Islands; $40,000 to the University of Lund for research in genetics and plant breeding; a five-year grant of $50,000 to the University of Uppsala to provide technical assistance to Arne Tiselius in his new headquarters at the Biochemical Institute; and $20,000 to the Haskins Laboratories, New York, for research in protozoological chemistry under S. E. Hutner. Numerous grants were given for research equipment, assistance, or visits.

In the Laboratories

Battelle Memorial Institute has laid the cornerstone (which included the usual "time capsule") for its new research center at Frankfurt/Main and has announced that it will establish another center at Geneva. A program of fellowships for students in German and Swiss universities is planned, those in Germany to be administered by the Stifterverband fur die Deutsche Wissenschaft, e. V., and those in Switzerland by the Swiss Federal Institute of Technology. The site for Battelle-Frankfurt was donated by the city of Frankfurt.

Bell & Howell Company was the first-place winner in the Industrial Management Society's second Methods Improvement Competition. Second and third prizes were awarded to the **Birtman Electric Company,** of Rock Island, Ill., and the **Upjohn Company,** of Kalamazoo, Mich. Awards were presented at the annual National Time and Motion Study Banquet in Chicago.

El-Tronics, Inc., has expanded its research and industrial facilities in Philadelphia by the acquisition of an additional 17,000 square feet of space at Fifth & Noble Sts.

The **Encephalitis Investigations Unit** of the Public Health Service has been transferred from Kansas City, Kan., to Greeley, Colo., summer headquarters for field work. Early in 1953 a section of the **Virus Laboratory** at Montgomery, Ala., will be established in Greeley, thus unifying field and laboratory studies.

A new scientific center for the British lace industry is the **Lace Research Association's** new laboratories at Bilborough, Nottingham. The center will seek to improve methods of production, the range of goods, and mechanical productivity. Its work is financed in part by the proceeds of a statutory levy from all the manufacturing sections of the trade, in part by subscription, and by a government grant based on the amount of money raised in the industry.

Lederle Laboratories Division, American Cyanamid Company, has added Sherman L. Burson, Jr., of Pittsburgh, to the staff of the Organic Chemistry Department, and Marvin Rosen to the staff of the Chemical Research Department.

The **National Cancer Institute** of the National Institutes of Health has established two new branches—the Research Medicine Branch, under Roy Hertz, chief; and the Clinical Medicine and Surgery Branch, under Robert R. Smith, acting chief. Dr. Hertz was head of the former Endocrinology Branch, and Dr. Smith has recently been appointed chief surgeon of National Cancer Institute.

Meetings and Elections

The **American Academy for Cerebral Palsy,** at its annual meeting in Durham, N. C., elected the following officers: president, Arnold Gesell; president-elect, Meyer A. Perlstein; secretary-treasurer, Harry E. Barnett.

The **American Society of Photogrammetry** will hold its annual meeting Jan. 14–16 at the Shoreham Hotel, Washington, D. C. A panel on "Arctic Mapping," a joint Canadian and U. S. project will be one of the high lights. One day will be devoted to photo interpretation and its applications to science, industry, and military intelligence. A preprogram tour of the Engineer Research and Development Laboratories, Fort Belvoir, Va., will be conducted Jan. 13 for those registered prior to that date. Louis J. Reed, 201 Wellington Dr., Alexandria, Va., is chairman of the Program Committee.

A symposium on **Automatic Computing Equipment in Industry** will be held in Kansas City, Mo., Jan. 8–9. It will be sponsored by Midwest Research Institute in cooperation with local sections of the American Society of Mechanical Engineers, the American Society of Civil Engineers, American Institute of Chemical Engineers, Instrument Society of America, American Institute of Electrical Engineers, Institute of Radio Engineers, and the Society of Automotive Engineers. Representatives from industry, government, and education will attend and participate in the program. A complete digest of the program may be obtained from Martin Goland, Midwest Research Institute, 4049 Pennsylvania, Kansas City, Mo. Advance registration is requested.

The eighth **International Medical Cruise Congress** of the Pan American Medical Association will sail from New York on the S. S. *Nieuw Amsterdam* Jan. 7 and return to New York Jan. 19. The ship will touch at Port-au-Prince, Cartagena, Cristobal, and Havana. Scientific sessions will be held each morning while the ship is at sea, and there will be panel discussions on special subjects.

Officers elected by the **Society of Motion Picture and Television Engineers** for two-year terms beginning Jan. 1 are: president, Herbert Barnett; vice presidents, John G. Frayne, Norwood L. Simmons, and John W. Servies; secretary, Edward S. Seeley. Henry J. Hood, of Eastman Kodak Company, assumed office as engineering vice president, filling the vacancy created by the resignation of F. T. Bowditch.

A **Symposium on Pain** will be an outstanding feature of the midwinter meeting of the American Academy of Dental Medicine at the Hotel Statler, New York, Dec. 7. Participants will be Nathan Savitsky, Theodor Blum, and Samuel Charles Miller. Joseph L. Bernier will act as moderator. For full information, address the national secretary, William M. Greenhut, 124 E. 84th St., New York 28.

Miscellaneous

The **American Cancer Society** presented its 1952 Distinguished Service Award posthumously to Howard W. Blakeslee, science editor of the Associated Press, in ceremonies held Nov. 12 in New York.

The **University of Chicago** and the **Chicago Association of Commerce and Industry** will sponsor a ceremony and luncheon on Dec. 2, anniversary of the first self-sustained nuclear chain reaction. Enrico Fermi, Lawrence A. Kimpton, and Arthur H. Compton will speak at the Stagg Field ceremony, and Dr. Compton will be the luncheon speaker. His topic will be "Atomic Power: Its Birth and Its Human Values." Immediately following the luncheon, there will be a panel discussion on "Industrial Uses of Atomic Energy in the Next Ten Years," of which C. H. Greenewalt will be moderator. Other panel speakers will be Walter H. Zinn, Lawrence R. Hafstad, W. Allen Wallis, Charles A. Thomas, Murray Joslin, and Drs. Fermi and Compton.

At the Belfast meeting of the British Association for the Advancement of Science, the Duke of Edinburgh, BAAS immediate past president, presented the **Endeavour Prizes.** First prize went to Aileen Forest, assistant lecturer in zoology at the University of Aberdeen, for an essay on "The Origin of Life." A. Gilchrist, of Magdalen College, Oxford, who will soon start postgraduate work at Brown University, won second prize, and R. V. Coates won third prize. Two prizes to junior scientists (under 18) were awarded to Ivor Johnson, of Wallasey Grammar School, and to Soli Lam, an Indian student at Dulwich College.

Selman Abraham Waksman, Rutgers University microbiologist, was awarded the **Nobel Prize** for medicine and physiology by the Council of the Caroline Institute of the University of Stockholm for his work in the discovery of streptomycin. The prize is worth $33,200 this year. The citation accompanying the award said streptomycin was the first effective antibiotic found for use against tuberculosis. The chemistry prize was shared by two British biochemists, Archer J. P. Martin and R. L. Millington Synge, for the development of the partition chromatography process. Edwin Mills Purcell, of Harvard, and Felix Bloch, of Stanford, won the physics prize for their development of new methods for nuclear magnetic precision measurements and their discoveries in this field.

Chemicals wanted by the **Registry of Rare Chemicals,** 35 W. 33rd St., Chicago 16, include: sodium rhodium chloride; magnesium boride; beryllium molybdate; 2,5-diphenyl oxazole; 1,2,3,4-tetrahydrooxine; 2,3,4-trihydroxybenzalaniline; tetramethylthionine; benzophenone-2,2'-dicarboxylic acid; 3-chloro-1-butanol; cis-cinnamaldehyde: 2,4-decadienal; mellitic acid; pseudopellitierine; β-naphthyl hydrazine hydrochloride; hydrocoerulignone; ecgonine; fainesene; ocimene; tropine; and xanthotoxin.

Technical Papers

The Reduction of Tetrazolium Salts by an Isolated Bacterial Flavoprotein[1]

Arnold F. Brodie[2] and Joseph S. Gots

Department of Microbiology, School of Medicine, University of Pennsylvania, Philadelphia

In a previous publication (*1*) the authors demonstrated that 2,3,5,triphenyltetrazolium chloride (TTC) could be enyzmatically reduced by the yeast flavoprotein, diaphorase, with the simultaneous oxidation of a molar equivalent of reduced DPN. Recently, Kun (*2*) presented evidence which clearly demonstrated that other flavin enzymes (i.e., amino acid oxidases) could also reduce this compound. He could not demonstrate the reduction of TTC with glycolytic enzymes unless mitochondrial fractions were added. Shelton and Schneider (*3*) were able to show that purified xanthine oxidase, and diphosphopyridine nucleotide-cytochrome *c* reductase, were able to reduce tetrazolium salts rapidly. The present investigation was undertaken with an isolated bacterial enzyme which could reoxidize reduced DPN concurrently with the reduction of TTC or neotetrazolium (NTC).

Mattsen *et al.* (*4*) reported the reduction of TTC by a glucose dehydrogenase–coenzyme I linked system, but it was not mentioned whether flavin enzymes were involved. In a later publication Jensen *et al.* (*5*) reported that the tetrazolium salts could be reduced by a series of DPN linked dehydrogenase enzymes, including lactic and phosphoglyceraldehyde dehydrogenases. They claimed that these systems did not contain flavoproteins or cytochrome oxidase, although no experimental data were presented to support this conclusion. In a previous publication (*1*) we investigated the ability of phosphoglyceraldehyde dehydrogenase to reduce TTC. Under the conditions of the experiment the formazan was not produced. We have continued the dehydrogenase study with crystalline lactic dehydrogenase isolated from rabbit muscle according to the method of Korkes *et al.* (*6*), alcohol dehydrogenase isolated from yeast according to the method of Racker (*7*), and glycerol dehydrogenase isolated from *Escherichia coli* by the method of Asnis and Brodie (unpublished). The reduction of DPN was followed spectrophotometrically at 340 mμ in the Beckman spectrophotometer (model DU), and in no instance did the tetrazolium salts interfere with this reduction. The formation of formazan and diformazan was followed at 485 mμ and at 530 mμ, respectively, with no evidence of formazan production by any of the dehydrogenases tested.

An enzyme was extracted from *E. coli* strain ECFS, which could reoxidize reduced DPN (*8*). The cells were disrupted by sonic vibration and fractionated with ammonium sulfate. The yellow enzyme showed a typical flavin spectrum when analyzed in the spectrophotometer. This oxidase had no other dehydrogenase activity and was inactive with TPN reduced with glucose-6-phosphate and its dehydrogenase.[3]

This enzyme behaved similarly to yeast diaphorase in that it could reduce TTC and NTC in the presence of reduced DPN. The pH optimum for this reduction with the bacterial enzyme was found to be 7.8. The reduction of neotetrazolium could now be reconstituted enzymatically with various fractions from one organism. In Fig. 1, DPN was reduced with the glycerol

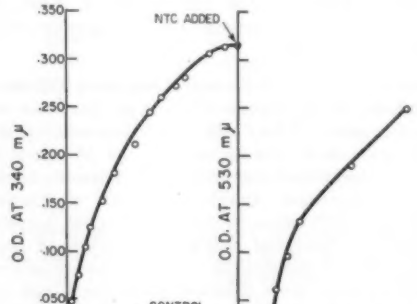

FIG. 1. The reduction of neotetrazolium by bacterial fractions. The system consisted of 500 μg DPN, 30 μM glycerol, 0.5 ml glycerol dehydrogenase, 1 ml *M*/10 pyrophosphate buffer pH 7.8, and distilled water to make a final volume of 3 ml. After the reduction of DPN had reached a plateau, 100 μg NTC was added and followed at 530 mμ for 15 min, whereupon 0.1 ml bacterial oxidase (S. Ext. 20.5) was added.

dehydrogenase fraction isolated from *E. coli* (ECFS). Upon the addition of NTC no reduction occurred during a 15-min period. When the oxidase fraction of the same organism was added, the reduction of NTC (and the simultaneous reoxidation of reduced DPN) occurred. Two moles of reduced DPN were found to be necessary for the reduction of one mole of NTC—i.e., 0.10 μM of reduced DPN were oxidized for 0.056 μM of neotetrazolium reduced.

To characterize the prosthetic group of the enzyme, the following method was employed. Manometric experiments were performed in which the oxygen uptake was followed with reactivated D-amino acid oxidase apoenzyme prepared from pig kidney.[4] Various con-

[1] This work has been aided by a grant from the Eaton Laboratories, Inc., Norwich, N. Y.

[2] Present address: Biochemical Research Laboratory, Massachusetts General Hospital, Boston.

[3] The reduced TPN was kindly supplied by Dwight B. McNair Scott, of Children's Hospital, Philadelphia.

[4] The D-amino acid oxidase apoenzyme and flavin adenine dinucleotide (95% of the total flavin present) were generously supplied by Leslie Hellerman, of the Johns Hopkins Medical School.

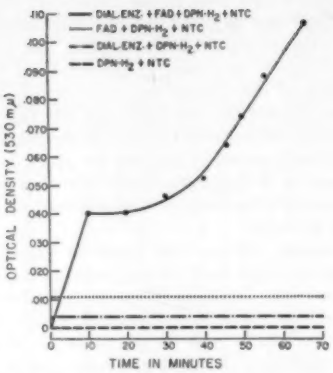

FIG. 2. Reactivation of bacterial oxidase after dialysis in dilute HCl. The system consisted of 0.5 ml bacterial enzyme, 24 μg FAD, 100 μg neotetrazolium, 1 ml *M*/10 pyrophosphate buffer pH 7.8, and distilled water; incubated for 10 min before the addition of 1000 μg reduced DPN to make a final volume of 3 ml. Control systems are indicated.

centrations of flavin adenine dinucleotide (FAD) were added in order to determine the rate of oxygen uptake as a function of the flavin concentration. The flavin content of the hydrolyzed bacterial oxidase was then determined in the same manner. It was capable of reactivating the D-amino acid oxidase apoenzyme. The nonhydrolyzed enzyme failed to reactivate the oxidase.

Although the data indicated the presence of FAD, it seemed essential to demonstrate the necessity of this coenzyme for enyzmatic activity. By dialyzing the bacterial enzyme for 24 hr in the presence of dilute HCl and potassium monobasic phosphate, similar to the method of Warburg and Christian (*9*), an apoenzyme was prepared which was inactive in the presence of reduced DPN and neotetrazolium (Fig. 2). When FAD was incubated with this apoenzyme, the system was reconstituted, and about 60% of the original activity was recovered. Neither reduced DPN nor FAD, alone or combined, could reduce the neotetrazolium.

By limiting the addition of flavin (Fig. 3), it was found that the amount of diformazan produced is a function of the concentration of added FAD. Experiments were performed in which the rate constant in

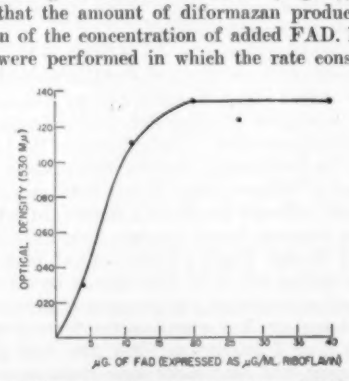

FIG. 3. Effect of various concentrations of FAD on bacterial oxidase after dialysis in dilute HCl. (Conditions same as in Fig. 2.)

mole^{-1} min^{-1} liter was determined for the oxidation of the bacterial enzyme with neotetrazolium and oxygen (*10*). The bacterial enzyme was found to have a greater turnover when neotetrazolium was used as an electron acceptor. The rate of reaction of neotetrazolium was similar to the rate of reaction of ordinary redox dyes such as methylene blue.

In bacteria the reduction of tetrazolium salts has been shown to occur in discrete granules (*11*). *In vitro* this reduction with isolated bacterial enzymes can be accomplished by flavin enzymes. Neither DPN-dehydrogenases nor reduced DPN, per se, can reduce these salts to the formazan state.

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The Grafting of Large Monocotyledonous Plants

Thomas J. Muzik and Carl D. La Rue

Federal Experiment Station, Mayagüez, Puerto Rico, and Department of Botany, University of Michigan, Ann Arbor

The grafting of plants has been a common horticultural practice for many centuries. For almost as great a stretch of time two ideas have been associated with this practice: first, that monocotyledonous plants cannot be grafted; and second, that leaves cannot be grafted. As late as 1947, Transeau, Sampson, and Tiffany (*1*) stated, "Neither twig grafting nor budding is possible in stems without cambiums." For successful union it was stated by Eames and McDaniels (*2*) that the cambium of the scion must be united with that of the stock. Similar expressions may be found in dozens of textbooks.

In 1946 La Rue and Reissig (*3*) reported that leaves of numerous species could be grafted and found that fleshy leaves required a technique different from that used with thin ones.

Calderini (*4*) reported, more than a hundred years ago, that he had made successful grafts of rice on barnyard grass. He claimed that by this means he had produced a new strain of rice with superior characteristics which, thereafter, were transmitted by the seeds. The latter statement, however, brings into question the validity of the entire paper. Plotnikov (*5*) made grafts in grains, and Monakima and Solevey (*6*) grafted

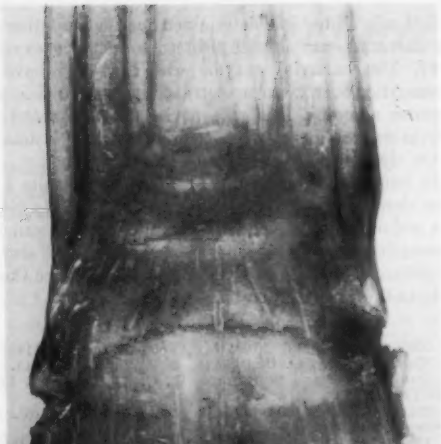

FIG. 1. Longitudinal section of a sugar-cane stem, showing union between scion and stock, 30 days after grafting. Some vascular connections between stock and scion are now established.

monocotyledonous bulbs. La Rue (7), without knowledge of the work of the three preceding investigators, grafted species of *Tradescantia, Zebrina,* and *Commelina.* He proved that the vascular bundles of stock and scion could unite when pieces of broken intercalary meristems on stock and scion were fastened in contact with each other.

In spite of the preceding records of success, no one, so far as the authors are aware, has successfully grafted any of the larger monocotyledons. Although cambiums are not usually found in monocots, or are limited in amount and confined to unusual locations, such as bulbs, corms, etc., other meristems do occur. The most important of these in this study was the intercalary meristem, a region just above the node which retains its meristematic qualities long after the rest of the stem is mature. By appropriate manipulation of this structure, successful grafts of bamboo (*Bambusa longispiculata* Gamble ex Brandis), sugar cane (*Saccharum officinarum* L.), guinea grass (*Panicum maximum* Jacq.), and Merker grass (*Pennisetum purpureum* Schum.) were obtained. On the average about 3% of the grafts were successful.

The method used was very simple. The shoot was grasped firmly and broken with a quick jerk. The young, thin-walled cells in the intercalary region are weaker than the adjacent mature thick-walled cells, and the rupture occurs in this region. The same stem may be replaced, or a stem of the same size from another plant of the species may be inserted. An exact fit is very important, but trimming the edges of the graft proved deleterious. In most of the plants tested, the leaf sheath served to support the graft. It was advantageous to tie the grafts firmly to ensure even, continuous contact. Best results were obtained with young, vigorous material.

Histological sections were made at various stages of the graft union and stained with fast green and safranin. At the junction of stock and scion a week after grafting there is a thin dark layer, which is probably formed in part by the remnants of cells injured in rupturing the stock and scion and in part by oxidation on the surfaces of cells torn apart but with walls left intact. Resorption of this contact layer occurs first between the ruptured vascular bundles and is more or less limited to these areas. Cell proliferation occurs simultaneously along the edges of both stock and scion, and a band of cambiumlike tissue is sometimes formed. In successful grafts, this layer is usually limited to a few tiers of cells. These parenchyma cells differentiate into short, lignified tracheids, with scalariform thickening, and reunite the vascular bundles. It is apparent that survival of the graft is dependent on the successful resorption of the contact layer, at least between the broken vascular bundles. Definite vascular connections were first observed about 4–6 weeks after grafting (Fig. 1).

During this period the scion remains green, but no elongation occurs. New growth occurs from terminal or axillary buds. In sugar cane, the scions sometimes formed roots, giving a fictitious appearance of successful union. After a successful graft begins to grow it sometimes continues at about the same rate as on intact plants, although on others it may be very slow. For example, one of the bamboo grafts grew approximately 10 ft in 8 months, whereas another stayed green but grew hardly at all over the same period. Grafted sugar-cane and guinea grass plants flowered at the same time as ungrafted plants.

Microscopic examination showed that in the rejoining of stock and scion, there was seldom perfect juxtaposition of the vascular bundles, and the reunion often took place in a curve, rather than a straight line. This is a clear demonstration of the influence of the vascular tissue on the proliferation and differentiation of parenchyma cells. Differentiation occurs both upward and downward, although mostly in a downward direction.

On the Solomon Island ivyarum, *Scindapsus aureus* (Lindl. & Andre) Engl., a large tropical liana, a different technique was used. This species does not have an intercalary meristem, but the actively growing tips remain more or less meristematic throughout the youngest 3 or 4 internodes. Such tips were grafted by inarching, and the unions were made in a transverse rather than a longitudinal direction. Other grafts on this plant were made by rupturing the young inter-

node as in the previously described experiments, but since these plants have no leaf sheaths, the graft was supported with waxed paper tubes slipped over the stump and scion, or with bamboo splints, which served to hold the broken edges in contact until union occurred. This suggests that other monocotyledonous species may also be grafted, even though they may lack an intercalary meristem.

It is doubtful that these techniques will soon find practical application, unless a greater percentage of success can be achieved, but they should be useful for certain types of investigation.

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Tables for Use in Fourfold Contingency Tests[1]

Donald Mainland and I. M. Murray

Division of Medical Statistics,
Department of Preventive Medicine,
New York University College of Medicine, and
Department of Anatomy, State University of New York, Medical Center, New York

Statistical tests are becoming more and more commonly used by professional research workers, technologists, and "occasional investigators" such as medical practitioners. Many of these workers, however, find the arithmetic irksome, and, when dealing with small samples, they are perturbed by the possibility that the simple familiar tests may be misleading. For some tests both these problems can be solved by tables that demand little or no computation by the user. The possible objection to such tables, that they will tend to reduce the investigator to a statistical automaton, does not, we think, apply to tables more than to tests that require calculation. Repetition of arithmetic does not increase insight into the meaning of tests, and reduction of arithmetic may allow emphasis to be placed where it should always be placed, on sampling and inference.

In order to solve the two problems reliability of verdicts and reduction of arithmetic, tables for use in contingency tests and in the estimation of binomial confidence limits were published in an article on statistical methods for medical research workers by the National Research Council of Canada in 1948 (*1*). That article is now out of print, but copies are still requested by workers in many branches of applied science. Revision and extension of the tables have therefore been undertaken, and the first two of the new series are presented here.

Purpose. These two tables are primarily for the comparison of equal samples, with individuals classified as *A* and not-*A*, and arranged in a fourfold contingency table; for instance: animals wounded by the same method and randomly allocated to two diets for comparison of fatality rates; two successive differential blood counts from the same patient to show a change in the neutrophil leukocyte percentage; samples of an industrial product made by two slightly different machines and examined for proportions defective; samples of tagged fish or birds liberated in different localities or under different conditions, for comparison of proportions subsequently recovered.

In each instance, if the investigator wishes to make allowance solely for random sampling (chance) variation he will ordinarily apply the chi-square contingency test, introducing for greater accuracy Yates' correction for continuity; or he may use an equivalent form of the standard error of the difference between two proportions. Owing to the smallness of samples or skewness of distributions, one or more of the expected values in the χ^2 calculation may be small, and the smaller the expected value the less dependable is the χ^2 test, even with Yates' correction. The investigator can apply certain empirical rules (*2*) to determine the safety of the test, and if it is unsafe he can do a further calculation and use Table VIII of Fisher and Yates (*3*). If that is insufficient he can calculate the exact probabilities (Fisher [*4*], Sec. 21.02).[2]

Our tables can be substituted for all these methods, even the initial χ^2 calculation, when the samples are equal and when, as is usually the case, the investigator requires only an assessment of significance at the conventional 5% and 1% levels—i.e., when the standards are $P = 0.05$ and $P = 0.01$, where P is the probability for χ^2 or the corresponding (two-tailed) exact probability.

Method of using the tables. Let us imagine two samples, *V* and *W*, each containing 30 individuals. *V* is composed of 17 *X*s and 13 *Y*s; *W*, 20 *X*s and 10 *Y*s. For ease in entering our tables, we form a contingency table, with the order of the samples changed, thus:

Sample	*Y* (*A*s)	*X* (not-*A*s)	Total (*N*)
(1) *W*	10	20	30
(2) *V*	13	17	30

The *W* sample, having the greater discrepancy between *X* and *Y*, is placed in the upper line and becomes Sample (1); and in that sample the smaller value, 10,

[1] This article is part of a biometrical tables project conducted in the New York University Division of Medical Statistics. For grants-in-aid of the project we are much indebted to the Abbott Laboratories, the Milbank Memorial Fund, Parke, Davis & Company, Chas. Pfizer & Co., and the Squibb Institute for Medical Research. For carrying out nearly all the computations we wish to thank Catherine Mescal and Joan M. Hansen.

[2] Sometimes this method is incorrectly referred to as "the exact chi-square" method. The distinction can be illustrated in an elementary way by a sampling experiment (*2*).

TABLE 1

MINIMUM CONTRASTS REQUIRED IN FOURFOLD CONTINGENCY TABLES FOR SIGNIFICANCE AT THE 5% LEVEL

N	As in Sample (1)/As in Sample (2)
4	0/4 1/– 2/–
5	0/4 1/5 2/– 3/–
6	0/5 1/6 2/– 3/–
7	0/5 1/6 2/7 3/–
8	0/5 1/6 2/7 3/8 4/–
9	0/5 1/6 2/8 3/8 4/9
10	0/5 1/7 2/8 3/9 4/10 5/10
11	0/5 1/7 2/8 3/9 4/10 5/11
12	0/5 1/7 2/8 3/9 4/10 5/11 6/12
13	0/5 1/7 2/8 3/9 4/10 5/11 6/12
14	0/5 1/7 2/8 3/10 4/11 5/12 6/12 7/13
15	0/5 1/7 2/9 3/10 4/11 5/12 6/13 7/14
16	0/5 1/7 2/9 3/10 4/11 5/12 6/13 7/14 8/15
17	0/5 1/7 2/9 3/10 4/11 5/12 6/13 7/14 8/15
18	0/5 1/7 2/9 3/10 4/11 5/12 6/13 7/14 8/15 9/16
19	0/5 1/7 2/9 3/10 4/11 5/12 6/14 7/14 8/15 9/16
20	0/5 1/7 2/9 3/10 4/11 5/13 6/14 7/15 8/16 9/16 10/17
30	0/6 1/8 2/9 3/11 4/12 5/13 6/15 7/16 8/17 9/18 10/19 15/24
40	0/6 1/8 2/9 3/11 4/12 5/14 6/15 7/16 8/18 9/19 10/20 20/30
50	0/6 1/8 2/10 3/11 4/13 5/14 6/15 7/17 8/18 9/19 10/20 11/22 25/36
60	0/6 1/8 2/10 3/11 4/13 5/14 6/16 7/17 8/18 9/20 10/21 11/22 12/23 13/24 14/26 /15/27 30/42
70	0/6 1/8 2/10 3/11 4/13 5/14 6/16 7/17 8/18 9/20 10/21 11/22 12/23 13/25 18/30 19/32 20/33 35/48
80	0/6 1/8 2/10 3/11 4/13 5/14 6/16 7/17 8/19 9/20 10/21 11/22 12/24 13/25 14/26 15/27 16/29 23/36 24/38 40/54
90	0/6 1/8 2/10 3/11 4/13 5/14 6/16 7/17 8/19 9/20 10/21 11/23 12/24 13/25 14/26 15/28 20/33 21/35 31/45 32/47 44/59 45/59
100	0/6 1/8 2/10 3/11 4/13 5/15 6/16 7/17 8/19 9/20 10/21 11/23 12/24 13/25 14/27 18/31 19/33 25/39 26/41 50/65
150	0/6 1/8 2/10 3/12 4/13 5/15 6/16 7/18 8/19 9/20 10/22 11/23 12/24 13/26 14/27 15/28 16/30 19/33 20/35 25/40 26/42 32/48 33/50 41/58 42/60 75/93
200	0/6 1/8 2/10 3/12 4/13 5/15 6/16 7/18 8/19 9/21 10/22 11/23 12/25 13/26 14/27 15/29 18/32 19/34 22/37 23/39 27/43 28/45 33/50 34/52 41/59 42/61 51/70 52/72 65/85 66/87 100/121
300	0/6 1/8 2/10 3/12 4/13 5/15 6/16 7/18 8/19 9/21 10/22 11/24 12/25 13/26 14/28 15/29 16/30 17/31 18/33 19/34 20/35 21/37 24/40 25/42 29/46 30/48 35/53 36/55 41/60 42/62 48/68 49/70 56/77 57/79 66/88 67/90 78/101 79/103 95/119 96/121 150/175
400	0/6 1/8 2/10 3/12 4/13 5/15 6/17 7/18 8/19 9/21 10/22 11/24 12/25 13/26 14/28 15/29 16/30 17/32 20/35 21/37 24/40 25/42 28/45 29/47 33/51 34/53 38/57 39/59 44/64 45/66 51/72 52/74 58/80 59/82 67/90 68/92 76/100 77/102 87/112 88/114 100/126 101/128 117/144 118/146 141/169 142/171 200/229
500	0/6 1/8 2/10 3/12 4/13 5/15 6/17 7/18 8/19 9/21 10/22 11/24 12/25 13/26 14/28 15/29 16/30 17/32 18/33 19/34 20/36 23/39 24/41 27/44 28/46 32/50 33/52 37/56 38/58 42/62 43/64 48/69 49/71 55/77 56/79 62/85 63/87 70/94 71/96 79/104 80/106 89/115 90/117 100/127 101/129 113/141 114/143 128/157 129/159 147/177 148/179 172/203 173/205 250/282

is placed on the left and classified as "A." We now take from this table the pair of figures 10/13 and enter Table 1 at $N = 30$. There we find 10/19, which means that, corresponding to 10 As in Sample (1), we require in Sample (2) at least 19 As for significance at the 5% level. Our observed difference, therefore, is not significant.

If, instead of 10/13, the observed contrast had been 10/20, the differenee would have been significant at the 5% level; but Table 2 shows that it would not have been significant at the 1% level, which requires at least 21 As in Sample (2) for contrast with 10 in Sample (1). (Entries such as "2/–" at $N = 4$ in Table 1 indicate that, however much the number of As in Sample (2) was increased, even as far as N itself, the contrast could not reach the level of significance. For N less than 4, no entries are given, because with samples of 3 or less the 5% level cannot be reached. Likewise, in Table 2 no entries are given for N less than 5.)

Interpolation. To save space, many entries have been omitted, but they are easily supplied. Thus, at $N = 30$ in Table 1 there is a gap between 10/19 and 15/24, but it will be noted that the difference between 10 and 19 is 9, the same as the difference between 15 and 24. The missing items are therefore: 11/20, 12/21, 13/22, and 14/23.

Interpolation between values of N will seldom cause serious doubt. If two samples, each with 320 individuals, contained, respectively, 92 and 117 As, we should find from Table 1 that the contrast for $N = 300$ is 92/116, and for $N = 400$, it is 92/118. We should conclude that the difference between our samples was in the neighborhood of significance at the 5% level, with P more likely to be less than 0.05 rather than greater, because 320 is nearer to 300 than to 400. This would be correct, because χ^2 (with Yates' correction) for the observed samples is 4.092, which Table VIII of Fisher and Yates shows to be significant.

Again to save space, the values of A in Sample (1) are not carried beyond half the sample size. Let us consider, therefore, samples with $N = 190$. One contains 80 *A*s and 110 not-*A*s; the other, 100 *A*s and 90 not-*A*s. For $N = 200$ the minimum contrast in Table 1 is found by interpolation between 66/87 and 100/121. In both of these the difference is 21; therefore, the required contrast is 80/101, which is greater than the observed contrast, 80/100. This might suffice for our purpose, for it would indicate that the observed difference was in the neighborhood of significance. We can, however, obtain a closer estimate by the following procedure, which, although at first sight apparently somewhat complicated, soon becomes automatic.

Looking at $N = 150$, we find that the last entry is 75/93, but we require a value of the form $80/x$, where x is greater than 80. We therefore visualize a fourfold table of the form:

80	70	150
> 80	< 70	150

Here the lower line contains the greater discrepancy, and so, rearranging the samples as in our first example, we look under $N = 150$ for a contrast of the form $< 70/70$. Obviously it must lie between the last two entries, and the difference there—e.g., in 42/60—is 18. Therefore the required contrast is 52/70. The second line of the above fourfold table thus becomes 98; 52; 150. Summarizing, we have for $N = 150$: 80/98; for $N = 200$: 80/101. Interpolating linearly, we should estimate that for 80/100 the corresponding value of N should be about 184. Our actual N is 190;

TABLE 2

MINIMUM CONTRASTS REQUIRED IN FOURFOLD CONTINGENCY TABLES FOR SIGNIFICANCE AT THE 1% LEVEL

N	*A*s in Sample (1)/*A*s in Sample (2)
5	0/5 1/– 2/–
6	0/6 1/– 2/– 3/–
7	0/6 1/7 2/– 3/–
8	0/6 1/8 2/8 3/– 4/–
9	0/6 1/8 2/9 3/9 4/–
10	0/7 1/8 2/9 3/10 4/– 5/–
11	0/7 1/8 2/9 3/10 4/11 5/–
12	0/7 1/8 2/10 3/11 4/11 5/12 6/–
13	0/7 1/9 5/13 6/13
14	0/7 1/9 6/14 7/14
15	0/7 1/9 7/15
16	0/7 1/9 2/10 3/12 4/13 5/14 6/14 8/16
17	0/7 1/9 2/11 7/16 8/16
18	0/7 1/9 2/11 8/17 9/17
19	0/7 1/9 2/11 9/18
20	0/7 1/9 2/11 4/13 5/15 6/16 7/16 10/19
30	0/8 1/10 2/12 3/13 4/15 10/21 15/26
40	0/8 1/10 2/12 3/14 4/15 5/17 8/20 9/22 19/32 20/32
50	0/8 1/10 2/12 3/14 4/15 5/17 6/18 7/20 9/22 10/24 25/39
60	0/8 1/10 2/12 3/14 4/16 5/17 6/19 8/21 9/23 11/25 12/27 19/34 20/36 24/40 25/41 26/41 30/45
70	0/8 1/10 2/12 3/14 4/16 5/17 6/19 7/20 8/22 10/24 11/26 14/29 15/31 21/37 22/39 32/49 33/49 34/50 35/51
80	0/8 1/10 2/12 3/14 4/16 5/18 6/19 7/21 9/23 10/25 12/27 13/29 16/32 17/34 24/41 25/43 38/56 39/56 40/57
90	0/8 1/10 2/12 3/14 4/16 5/18 6/19 7/21 8/22 9/24 11/26 12/28 15/31 16/33 19/36 20/38 28/46 29/48 43/62 44/62 45/63
100	0/8 1/10 2/13 3/14 4/16 5/18 6/19 7/21 8/22 9/24 10/25 11/27 14/30 15/32 18/35 19/37 23/41 24/43 33/52 34/54 47/67 48/67 49/68 50/69
150	0/8 1/11 2/13 3/15 4/16 5/18 6/20 7/21 8/23 9/24 10/26 11/27 12/29 14/31 15/33 17/35 18/37 21/40 22/42 26/46 27/48 31/52 32/54 39/61 40/63 51/74 52/76 75/99
200	0/8 1/11 2/13 3/15 4/16 5/18 6/20 7/21 8/23 9/24 10/26 11/27 12/29 13/30 14/32 16/34 17/36 19/38 20/40 23/43 24/45 26/47 27/49 31/53 32/55 36/59 37/61 43/67 44/69 51/76 52/78 63/89 64/91 100/127
300	0/8 1/11 2/13 3/15 4/17 5/18 6/20 7/22 8/23 9/25 10/26 11/28 12/29 13/31 15/33 16/35 17/36 18/38 20/40 21/42 23/44 24/46 27/49 28/51 31/54 32/56 35/59 36/61 40/65 41/67 45/71 46/73 51/78 52/80 58/86 59/88 66/95 67/97 76/106 77/108 88/119 89/121 107/139 108/141 150/183
400	0/8 1/11 2/13 3/15 4/17 5/18 6/20 7/22 8/23 9/25 10/26 11/28 12/29 13/31 14/32 15/34 17/36 18/38 19/39 20/41 22/43 23/45 26/48 27/50 29/52 30/54 33/57 34/59 37/62 38/64 41/67 42/69 46/73 47/75 52/80 53/82 57/86 58/88 64/94 65/96 71/102 72/104 79/111 80/113 88/121 89/123 98/132 99/134 111/146 112/148 127/163 128/165 152/189 153/191 200/238
500	0/8 1/11 2/13 3/15 4/17 5/18 6/20 7/22 8/24 9/25 10/27 11/28 12/30 14/32 15/34 16/35 17/37 19/39 20/41 22/43 23/45 25/47 26/49 28/51 29/53 32/56 33/58 35/60 36/62 40/66 41/68 44/71 45/73 49/77 50/79 54/83 55/85 59/89 60/91 65/96 66/98 72/104 73/106 79/112 80/114 86/120 87/122 95/130 96/132 104/140 105/142 115/152 116/154 127/165 128/167 141/180 142/182 159/199 160/201 184/225 185/227 250/292

therefore we should doubt if the contrast 80/100 would be great enough for significance. The exact probability, P, derived from the observed pair of samples is 0.0508. Therefore our conclusion that the difference did not quite reach the 5% level of significance would be correct. (Anyone who expects to use our tables frequently will find it helpful not only to fill in the gaps, but to write out the second half of the series for each value of N by the method just indicated.)

Application to unequal samples. For samples that are almost equal the tables are clearly of use; but even with more gross inequality they can give adequate verdicts regarding significance in two types of case:

1) When the smaller sample is enlarged to the size of the larger (with the original proportions of *As* and not-*As* unchanged) and Table 1 shows that the difference is not significant at the 5% level, it must be even farther from the significance level in the original samples—i.e., P must be even farther above 0.05. Thus, if a sample of 20 contains 5 *As* and a sample of 40 contains 15 *As*, we can imagine that the smaller sample is enlarged to contain 40 individuals of which 10 are *As*. With 10/15 we enter Table 1 at $N = 40$ and find that the minimum contrast necessary for significance is 10/20. The difference in the original samples is therefore not significant.

This method was applied to the data from an experiment in which 19 rabbits with a certain skin tumor had been treated by injection of a tumor extract. Eight rabbits with the same tumor had not been injected, and the results were:

	Tumors disappeared	Tumors persisted	Total
Injected	3	16	19
Not injected	0	8	8

Since it was known that spontaneous disappearance was possible, it was asked: Is there a significant difference between the two groups in the incidence of disappearance of tumors? Table 1 shows that, even if the second sample contained 19 rabbits instead of 8, the contrast 0/3 under $N = 19$ is far from significant at the 5% level.

2) When the larger sample is reduced to the size of the smaller (again with the original proportions unchanged) and the tables show that the difference is significant, it must a fortiori be significant in the original samples—i.e., P must be still farther below 0.05 (or 0.01).

It is of interest to apply this rule to the data on which Fisher (*4*) demonstrates the exact test. Among 13 criminals who were monozygotic twins, 10 had twin brothers or sisters who had been convicted. Among 17 criminals who were dizygotic twins, only 2 had twin brothers or sisters with records of conviction. In tabular form we have:

	Convicted	Not convicted	Total
Monozygotic	10	3	13
Dizygotic	2	15	17

To apply our tables by reducing 17 to 13, we should reduce 2 and 15 each by about one quarter of its original value; but here even this is unnecessary, for on entering Table 2 at $N = 13$ we find that 2/10 is significant at the 1% level. Therefore, for the actual samples, P must be much less than 0.01. The exact probability is in fact less than 0.001.

It is possible that, when a difference is on the verge of significance and there is considerable disproportion between the *As* and not-*As* in one or both samples, these two methods of approximate assessment might lead one astray; and so, where the verdict from them is not quite obvious, the full analysis (χ^2 or the exact probability test, as required) should be used. Even in these doubtful cases, however, the tables will enable one to decide whether calculation is necessary to reach a verdict.

Information on required sample sizes. The tables help, also, to indicate sample sizes that may be required to establish significance when the observed difference is not significant, but we assume, nevertheless, that a real (population) difference exists. With samples of 20 containing, respectively, 4 *As* and 7 *As*, the difference is far from significant at the 5% level. If, on increasing the sample size, we found that the proportions remained the same as in the samples of 20, we should need two samples of about 100 to give a significant difference, for the contrast then would be 20/35, and at $N = 100$ the contrast 20/34 is sufficient.

Preparation and reliability of the tables. For N up to 20, the entries, obtained from exact probabilities, have been extracted from the tables published previously (*1*). For samples of 30 onward, χ^2 with Yates' correction was commonly used, and its significance was assessed by Table VIII of Fisher and Yates (about 1850 χ^2 values); but where there was any doubt the exact probabilities were calculated (300 computations). In certain parts of the series it was found that the differences between adjacent entries, as exemplified above, were so constant that χ^2 (or probability) calculations were required only at intervals. (A large number of the entries omitted from the tables were, however, actually calculated, and interpolation can be considered safe.)

When exact probabilities were obtained we were impressed by the accuracy of the Fisher and Yates table. For this reason and also because of the methods, direct and indirect, employed in checking the computations, we believe that incorrect assessments in our tables must be rare, and, as they will be borderline cases, the resulting error of judgment will be negligible.

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"Polluted" Water from the Leaching of Igneous Rock[1]

Robert S. Ingols and Alfred T. Navarre[2]

Department of Sanitary Chemistry and Geology, Georgia Institute of Technology, Atlanta

Unpolluted surface and ground waters in the uplands of northern Georgia have been found to contain substantial concentrations of fixed nitrogen. Since nitrogen concentration has long been used as an index of water pollution, the observation of concentrations of 1.5–2.0 ppm in a small mountain stream at a point 2500 ft above sea level aroused our curiosity. After some study, we believe that this and numerous other observed occurrences of fixed nitrogen in presumably unpolluted waters of the area can be attributed to leaching of soluble nitrogen compounds from granite during weathering. A brief account of the investigation leading to this conclusion is presented here.

A series of analyses of well waters in the Atlanta area showed that many of them were extremely high in nitrogen as either ammonia, nitrite, or nitrate. One flowing spring under a large hotel in the city contained 40 ppm nitrate nitrogen. However, high nitrogen values in the city could possibly be explained by the use of lawn fertilizers or the presence of packing houses or dairy barns. On the other hand, when a small mountain stream and a spring that is tributary to it showed a nitrogen content of 1.5 ppm, it was evident that some natural cause might be responsible. The high value of nitrogen in the stream is approximately 100 times the nitrogen value for good drinking water.

A search of the geological literature did not disclose why the stream and well waters in northern Georgia should contain such high nitrogen values. However, since ammonium chloride is a commonly dispersed gas in the fog of volcanoes, it appears that it is fairly abundant in the interior of the earth. Thus, where the interior rocks now appear at the surface, ammonium chloride could have been included in them at the time they were formed.

The authors considered the hypothesis that the rapid rate of weathering of the granite rock in this area can be explained by leaching of trace amounts of soluble substances such as ammonium carbonate or ammonium chloride. With this in mind, pieces of igneous rock that had weathered both rapidly and slowly were brought into the laboratory, crushed, and then leached with a fairly large amount of water. The leachings were analyzed for the ions of ammonia, calcium, magnesium, chloride, nitrate, and carbonate. An attempt was made to determine whether soluble substances were present in higher amounts in rocks that weathered rapidly.

Results of a number of analyses of the leachings (Table 1) indicate that many igneous rocks yield soluble substances in approximately the same amount. Although some rocks weather at much more rapid rates than others, the rate of weathering of the rocks did not correlate with the fixed nitrogen value. Furthermore, an analysis of the leachings from some deeply weathered granite from northern Georgia near Clayton showed that the weathered residue still contained rather large amounts of easily leached ammonia. This fact is not well understood because, even though the rapid rate of weathering explains the high value for the ammonium chloride in the leached solution, it would be expected that the ammonium chloride should leave the rock during the early stages of weathering. However granite-gneiss also shows a high ammonium content, and yet it weathers very slowly.

The next question to be answered was the source of the ammonium chloride. It was possible that the nitrogen had been fixed from the atmosphere by the biological agencies in leguminous plants and then intruded into the rock from the ground water. A fresh sample of basalt (from 13,000 ft above sea level) from

TABLE 1

Sample	Location	pH	Carbonate system (mg/100 g)	Nitrogen (mg/100 g)	Chloride (mg/100 g)	Calcium plus magnesium (mg/100 g)
Hard unweathered	Clayton, Ga.	8.0	20	1.5	15	10
Partially weathered	" "	7.8	18	1.3	10	10
Decomposed granite	" "	8.2	15	1.2	12	8
Granite-gneiss	Toccoa, Ga.	6.3	22	1.5	25	12
Fresh basalt	Hawaiian Islands	6.8	420	2.3	70	64
Unweathered granite-gneiss	Lithonia, Ga.	9.3	72	1.8	58	30
" Granite	Mount Airy, N. C.	9.3	95	5.4	50	25
" "	Isle, Minn.	9.4	122	2.0	40	80
" "	Coneste, S. C.	8.0	40	8	14	84
" "	Atlanta, Ga.*	9.0	124	2.8	4	64
" "	" " †	8.3	7	1.8	54	18

* Hemphill Quarry on Northside Drive.
† Moreland Avenue, Southeast.

[1] Based on a paper presented at the Decatur meeting of the Georgia Academy of Science, April 1952.

[2] The authors wish to express their appreciation to the University Center of Atlanta Universities for their allocation of financial aid from Carnegie Foundation funds.

the recent eruption of Mauna Loa in the Hawaiian Islands was obtained from the territorial geologist. When this sample was crushed and leached, it showed a nitrogen content that is typical of the rocks that were found in the Georgia area. It appears, therefore, that the nitrogen content of Georgia granite is typical of other igneous rocks. It is not surprising that the nitrogen content of granite has not been studied, because its content at 25 ppm is certainly lower than the normal analytical procedures of geochemistry would detect. Furthermore, nitrogen is not picked up on a spectrochemical analysis in the excited electric arc; therefore, the discovery reported in this paper was made possible only because of the use of solution chemistry from the rock rather than by the use of a direct analytical approach. This type of chemistry has led to important developments in the use of granite dust, which, when applied to land very low in vegetation because of lack of the soluble substances needed for plant growth, has transformed it into a rich and verdant area.[3] The increase in plant growth has obviously resulted from the presence of the calcium, magnesium, potassium, sodium, and ammonia that have been leached from the dust by the action of rain water.

Previous sanitary analyses of the Chattahoochee River, which has a normal flow of something over 1000 cfs, have not shown any large nitrogen content. However, it should be remembered that the large flow includes a heavy surface runoff, which is not typical of a small mountain stream flowing slowly over and through residual soil.

The conclusion seems warranted, therefore, that the concentration of soluble compounds in spring water or surface water that has a chance to flow slowly over granite is determined by the rate of rock-weathering. The nitrogen content of waters in an area where there is rapid weathering of granite cannot be used to determine the load of human pollution, as is frequently done in areas where granite weathering is very slow.

Manuscript received May 19, 1952.

[3] Anon. Granite Dust Builds Better Soil. *Org. Farmer*, **3**, 38 (Mar. 1952).

Production of Better Penicillin-producing Strains by Mutation Induced by Uranium Nitrate

M. L. Gattani

Government of Rajasthan, Bharatpur, India

Stakman, Daly, Gattani, and Wahl (*1*) have shown that addition of uranium nitrate to potato dextrose agar at the rate of 0.5–1.0 g/liter stimulated mutation in the cultivated mushroom *Agaricus campestris*, and both mutation and an unusual type of dissociation in the ordinary corn smut fungus, *Ustilago zeae*. They suggested that addition of uranium nitrate or other similar salts may be a simple and useful means of inducing desirable mutations in at least some microorganisms. The agar containing uranium nitrate is mildly radioactive, as determined by Alexander Hollaender, Oak Ridge National Laboratory (*1*). The present studies were undertaken with a view to obtaining some better penicillin-producing mutants from their parents by growing the fungus on media containing uranium nitrate.

Penicillium notatum chrysogenum strain 18, isolated by Gattani and Kaul (*2*) from Indian soil samples, and strain Minnesota X1612 were used for these studies. This strain was brought by the author from the Department of Plant Pathology, University of Minnesota, in 1946 and was stored in sterile sand at room temperatures in India.

The method followed for inducing mutants in these strains differed from that used by Stakman *et al.* The strains were first grown on potato dextrose agar medium containing 0.5 g uranium nitrate/liter. The actively growing mycelium was then transferred to media containing 1.0, 1.5, or 2.0 g uranium nitrate/liter. By growing the fungus first on a low concentration of uranium nitrate and subsequently transferring the fungal mycelium to media containing higher concentrations of uranium nitrate, the frequency of mutation, as evinced by the production of morphologically distinct sectors, was enhanced two to three times. When the fungus mycelium was transferred directly from potato dextrose agar to media containing higher concentrations of uranium nitrate, the growth of the fungus was inhibited, and number of sectors produced was comparatively less.

Strain 18 produced mutants that could be broadly classified as white, entirely mycelial, nonsporeforming, or green mutants. Some of the white mutants spontaneously produced secondary green mutants. In Minnesota X1612 the mutants were of different shades of green, no white mutants being produced in this strain.

Penicillin-producing ability of the mutants and their parents was compared by the plug method, described by Raper, Alexander, and Coghill (*3*). One mutant, 18G, from more than 30 mutants of strain 18 tested, showed increased penicillin production; the four radial series plugs of this mutant strain produced bigger circles than those produced by the four plugs of the parent strain. Similarly, the four radial series plugs of one mutant of Minnesota X1612, designated as X1612-C, gave bigger circles of inhibition than those produced by the parent strain.

Unfortunately, because of inadequate facilities and nonavailability of corn-steep solids, the mutants of Minnesota X1612 and strain 18 could not be tested by measuring the amount of penicillin produced under submerged conditions on that medium. However, mutant strains and the parent strains were grown on Czapex liquid medium in surface culture. The culture filtrate was assayed after the 6th, 7th, 8th, 9th, and 10th days of inoculation. Invariably, 1:100 dilutions of the culture filtrate from the mutant strains 18G and X1612-C produced consistently bigger lytic zones than those produced by the parent strains 18 and X1612,

TABLE 1

SIZE OF LYTIC ZONES PRODUCED BY THE PARENT STRAINS AND THEIR MUTANTS

Strain No.	Size of lytic zone in mm				
	6th day	7th day	8th day	9th day	10th day
Minnesota X1612	21	28	27.5	27	22
X1612-C	24	30.5	29.1	28.5	25
18	18	19	23.5	25	24
18G	19	20	25	27.2	26.3

respectively. This shows that they produced more penicillin than did their respective parents on Czapex Dox medium. Table 1 summarizes these results.

As a result of these investigations it appears that addition of uranium nitrate to nutrient media may be a simple means of inducing desirable mutations, with respect to penicillin-producing ability, in at least some strains of *P. notatum chrysogenum*.

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Culture of Cell Suspensions and some Results

Henry Grossfeld

340 Riverside Drive, New York City

In regular tissue cultures, the embryo extract used as a constituent of the culture medium contains a great variety of growth-promoting substances and, in all probability, a number of growth-controlling factors. It is prepared, as a rule, from the clear supernatant obtained by the centrifugation of minced embryos. Sometimes, in cultures made up with freshly prepared extract, small groups of living cells are seen to grow without apparent connection with the main cell colony. These, it seems, originate from scattered cells that persist in the extract after centrifugation.

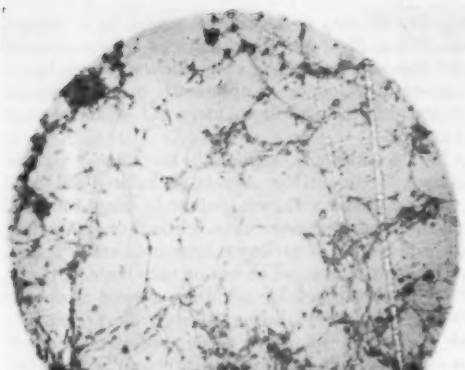
In an examination of this it has been found that in the centrifugation of minced embryos in the usual laboratory centrifuge, if no saline has been added, a clear supernatant is obtained only when the embryos are younger than 10 days. Ten- and 11-day-old embryos give an opaque, grey-white, viscous supernatant, and embryos older than 11 days under the same conditions of centrifugation give no supernatant in the usual sense at all. This opaque fluid contains a fine suspension of cells and may be used in culturing where the aim is to obtain diffuse cell growth without larger tissue explants.

Ten- or eleven-day-old chick embryos, thoroughly minced by small scissors, were centrifuged at a speed of approximately 2000 rpm for 20 min. The opaque viscous supernatant was spread in a film on a cover glass 30 × 30 mm, or larger, or placed in a culture flask. When the cover glass cultures were examined under the microscope, the suspension was seen to be composed of unconnected, apparently damaged, single cells and detrituslike cell splinters and a few isolated cell groups.

After 24–48 hr of incubation the microscopic picture had changed completely: Almost all isolated cells had become connected with one another by long, thin cell strands, or bridges, forming a continuous tissue network with meshes of various shapes and sizes (Figs. 1, 2). The growth area, which can be very large, depending on the area used for planting, showed variously differing cell clusters, distinguished by the preponderance of certain cell types, such as epithelial membranes, nerve cells, pigment cells, etc. When treated with a 1:40,000 solution of neutral red, all cells displayed normal vital staining. Frequently a culture would contain many single but normal-looking isolated cells which also showed normal vital granules. Some of those cells were seen in pairs as though adhering to one another after division. The most interesting feature of a suspension culture is the reticular growth which tends to connect, by filamentous long cell bridges, all cell groups into a continuous whole (Figs. 1, 2).

In a series of cultures, chicken plasma was added to the suspension on the cover glass, and clotting of the suspension was obtained. Growth of these cultures was likewise abundant, but the form of cell connections appeared strikingly different (Fig. 3). There was no visible reticulum. It would seem that differences in the physical character of the medium introduced by the plasma had had some influence on cell form and cell distribution. The difference displayed is one to be explored in a study of factors influencing tissue formation.

Suspension explants may also provide a means of approaching the problem of tissue reconstruction out of isolated cells. The following experiments illustrate this: Four parts of Ringer's solution was added to one part of the original cell suspension, thoroughly mixed, and centrifuged as indicated above. The now clear supernatant was removed, and the residue was again suspended in 4 parts of salt solution and centrifuged. This washing procedure was repeated 4 times, and thereupon the residue was suspended in Ringer's solution, from which suspension cultures were prepared. These cultures showed no signs of growth. In view of the fact that tissue fragments placed in Ringer's solution often are capable of producing cell growth in a regular tissue culture, the above result suggested that by the described washing procedure a substance might have been washed away which was responsible for the reticular tissue formation out of isolated cells. In support of this it was found that when various amounts of embryonic juice were then added to suspensions after having been washed as described, typical reticular tissue growth was obtained; this was the better the greater the concentration of embryonic juice



FIGS. 1 and 2. Cell suspension cultures. (Bouin; hematoxylin-eosin.)

in the suspension culture. By far the best growth of suspension explants was obtained when the residue was suspended in pure embryonic juice.

Two observations from these experiments may be considered: (*a*) The failure of suspension explants to grow without embryonic juice, whereas in regular tissue culture cell growth in pure Ringer's solution can be obtained; and (*b*) the capacity of pure, concentrated embryo juice to promote the growth of these cell suspensions, whereas in regular tissue cultures such concentrations are known to be inhibitory (*1, 2*).

In commenting on the first of these, the conclusion seems justified that suspension cultures need a greater amount of a substance present in embryonic juice and different from growth substances proper. This substance would appear to be the limiting factor for reconstructing reticular tissue out of isolated cells in suspension explants.

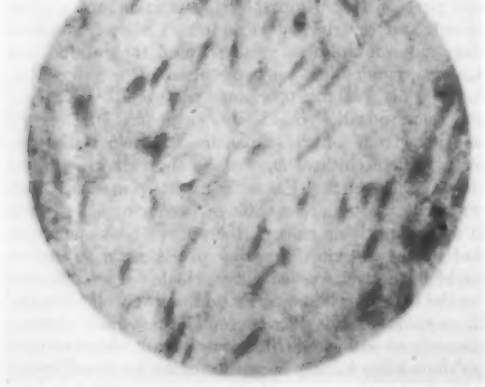


FIG. 3. Cell suspension culture grown in plasma clot. (Bouin; hematoxylin-eosin.)

At one time consideration was given to the possibility that this substance might be mucinlike—i.e., that amino sugars might be responsible for maintaining the adhesiveness of cell borders, or, in particular, that hyaluronic acid might possibly be functional in the formation of connective tissue. This substance, it was thought, might have been washed away by our washing procedure and would have to be replaced by a concentrated embryonic juice containing sufficient amounts of it. In support of that concept it has been shown that suspensions prepared from embryos with their eyes removed gave less reticular growth than when whole embryos were used. Eye tissues, in particular the corpus vitreum, obviously are rich in hyaluronic acid. However, the role that mucinlike substances, such as hyaluronic acid, may play in the formation of reticular growth in suspension cultures is yet far from being established.

The second of these observations can be explained in a natural way by the assumption that embryonic juice, besides containing substances that promote cell reproduction, also contains substances that encourage tissue formation while at the same time inhibiting cell reproduction. As soon as the concentration of embryo juice surpasses the optimum for cell growth, the higher concentration of growth-inhibiting substances in the concentrated embryo juice may become effective.

Because the suspension consists of cells forcibly torn out of the organized tissue units, and the regenerative capacities tend to reconstruct a new tissuelike cell organization, this method may provide another way of approaching the problem of the relationship between

reproduction and tissue formation. It provides, as well, a form of explanation without a central, partly necrotic tissue fragment, from which undefined substances are released into the medium such as to render it less suitable for quantitative determinations of metabolic processes.

It has been found that explanted suspensions containing cells originating from different organs, and from different animals, can form a cell reticulum and tissue continuity. This method can therefore be used for studying problems of protoplasmic specificity. There is some reason to justify the assumption that the method will prove convenient in providing a substrate of tissue for the propagation of viruses.

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A New Criterion for Weathering in Soils[1]

B. N. Rolfe and C. D. Jeffries

U. S. Geological Survey and School of Agriculture, The Pennsylvania State College, State College

Weathering consists of the mechanical disintegration and chemical deterioration of minerals at or near the ground surface. In soils, this process usually results in the development of a profile that may be described in terms of A, B, and C or D horizons. The greatest weathering occurs in the surface horizons, with a gradual decrease in intensity downward toward the parent rock. This simple picture of a soil profile is essentially that of a monogenetic soil defined by Bryan and Albritton (*1*) as one that has matured through a relatively uniform climate. Polygenetic soils (*1*) are those that have matured through at least two time intervals of different climates, with profile types superimposed one on the other. Such soils are not easily distinguished in the field. In addition, glacial, alluvial, and eolian depositions are common sources of superimposed profiles of weathering.

Differentiating between monogenetic and polygenetic profiles and recognition of buried profiles require distinction of the various soil horizons on the basis of an objective weathering criterion. This paper proposes such a criterion.

Recent studies by the authors have revealed a positive criterion for differentiating weathering regimes in a soil profile. The basis for this criterion is x-ray examination of the clay and silt fractions of the various horizons in the soil profile. If examination reveals the presence of mica minerals in either of these size fractions, the means are at hand for identifying the sequence of weathering. As this mineral group occurs so frequently in soils, the method of diagnosis should prove generally useful to pedologists and geologists.

Mica weathering is essentially a process of potassium depletion. Vadose water actively enters into hydrolytic interplay with the interface K^+ of the mica lattice. In the usual acid medium near the ground surface, this activity results in the displacement of this cation, with a consequent loosening of the bonding effect between mica sheets. Brown (*2*) has suggested

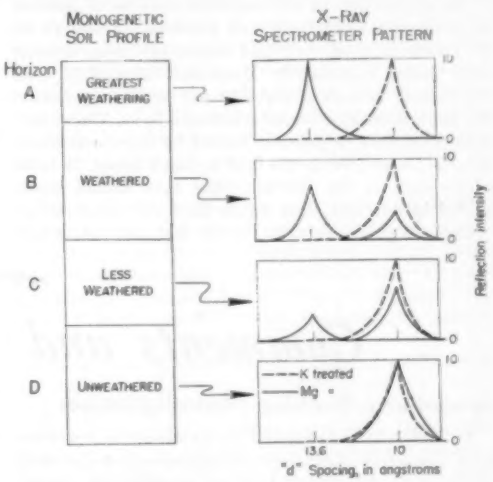

Fig. 1. Diagrammatic illustration of the weathering criterion.

the name "hydrous mica" for all those minerals that are hydrated micas, and the authors will follow this suggestion.

Mica in the unweathered state has a basal "d" spacing of 10 A, whereas the weathered, or hydrous, mica has a basal spacing that is directly dependent upon the saturating cation. In short, differential cation treatment of mica minerals will reveal the degree of weathering. Unweathered mica is tightly bonded by the interlayer cations and will maintain its 10 A basal spacing regardless of treatment. Weathering, however, with its accompanying cation depletion, results in a progressively greater response to differential cation treatment.

With respect to a monogenetic soil profile, the hydration effects of such divalent cations as Ca^{++} and Mg^{++} will be greatest in the A horizon and will gradually diminish toward the parent material. This is in accord with the concept that hydrous micas will dominate the surface horizon, whereas the D horizon will be composed of the unweathered, unhydrated form.

An example of such a monogenetic profile of weathering was first found in the Shackham Brook watershed located near Cortland, N. Y. The clays were saturated with 1 *N* MgAc (50 ml to 150 mg clay) and

[1] Contribution from the U. S. Geological Survey, Water Resources Division, and Department of Agronomy, The Pennsylvania State College, State College, Pa. Approved by the director, Geological Survey, and authorized for publication on May 13, 1952, as Paper #1734 in the Journal Series of the Pennsylvania Agricultural Experiment Station.

allowed to stand overnight on a steam bath. In the surface horizon where the hydrous mica was dominant, the basal spacing was 13.6 A. The amount of hydrous mica decreased consistently with depth until it was barely present in the fresh parent material. To prove that this spacing is merely the hydrated form of mica and not chlorite or montmorillonite, as sometimes reported, the same clays were then similarly treated with 1 *N* KAc. In all cases, the 13.6 A spacing was contracted to 10 A. Fig. 1 is a diagrammatic representation of this weathering sequence.

An application of this criterion may be of interest to geomorphologists and soil scientists. Thorp *et al.* (*3*), Schultz *et al.* (*4*), and others are using ancient soils (called paleosols by Hunt and Sokoloff [*5*]) as evidence of periods of stability and weathering during the deposition of river alluvium and loess. Under certain conditions, a paleosol buried by later deposition may be recognized in the field by dark bands. A technique such as the one described here should prove useful in differentiating bands that are the result of pedogenic processes from bands that may be caused by stratigraphic sequences of materials of varying texture, color, or consolidation.

Studies of kaolinite development in soils indicate a similar trend. Weathering and base depletion are greatest at the surface, and this is the zone of greatest kaolinite formation. Kaolinite thus serves as a corroborative check on hydrous mica with respect to weathering.

Application of the weathering criterion to a large number of agricultural soils in the U. S. has been made, and a detailed study will be published in a forthcoming paper.

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Comments and Communications

Sympathetic Blocking β-haloalkylamines

In 1949 (*1*) we reported the synthesis of a quaternary derivative of dibenzyl-(β-chloroethyl)-amine with a very high adrenergic blocking activity. Of special physiological interest was the rapid onset of the block, which was complete within a few minutes after intravenous administration in animal experiments (*2*). Further investigations on the substance supposed to be dibenzyl-(β-chloroethyl)ethyl-ammoniumbromide revealed that it must have another structure. The doubt concerning the quaternary nature of the compound was expressed in a communication by F. Lund (*3*) in connection with the delivery of an investigational sample, and quite independent of the observations made by J. F. Kerwin *et al.* (*4–6*). These authors stated that the compound (which we have called "Q") is identical with the hydrobromide of dibenzyl-(β-bromoethyl)-amine, when it is mixed to a slight degree (8%) with the hydrobromide of the corresponding chloro compound.

Elementary analyses on Q showed that it was not the expected quaternary derivative. Attempts to determine ionogenic Br^- failed, as it was impossible to obtain reproducible results.

Infrared spectrograms were then made by the Nujol mull technique. These showed a strong absorption around 3.9 μ that was unquestionably due to an amino salt grouping. Such an absorption is not shown by quaternary ammonium salts. On the other hand, the infrared spectrogram of pure dibenzyl-(β-bromoethyl)-amine hydrobromide was not identical with that of our preparation Q in the region of 7–13 μ. The bromo compound has a very strong absorption at 11.12 μ that is not at all represented in the Q spectrum. Instead, our substance Q has a spectrum that very closely resembles that of dibenzyl-(β-chloroethyl)-amine hydrobromide. In the spectra of some preparations, however, the absorption of the bromo compound at 11.12 μ (899 cm^{-1}) is obvious. It seems reasonable, therefore, to assume that our Q compound is chiefly dibenzyl-β-chloroethylamine hydrobromide mixed with the hydrobromide of dibenzyl-β-bromoethylamine. After several recrystallizations from a series of solvents, the end product is the bromo compound, dibenzyl-(β-bromoethyl)-amine hydrobromide.

In our animal experiments, both this compound and the Q-substance display very high adrenergic blocking activities. The temperature of the solvent used in the animal experiments, however, has a great influence on the activity; hence, a separation on a physiological basis seems very difficult.

E. Nyman
L.-O. Plantin
E. Östlund

Research Institute of King Gustaf V
Stockholm, Sweden

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The observations of Nyman, Plantin, and Ostlund on the reaction of dibenzyl-β-chloroethylamine with ethyl bromide are in substantial agreement with the results we reported, except with regard to the relative amounts of chloro and bromo compound in the mixture obtained from the reaction. Our mixture which, on the basis of analyses, we estimated to contain 92% of bromo compound absorbs at 11.12 μ (Nujol mull), as did some of the preparations of Nyman and co-workers. One recrystallization with a recovery of 86% gave a compound which possessed an infrared absorption spectrum identical with that of an authentic specimen of dibenzyl-β-bromoethylamine hydrobromide. Evidently Nyman, Plantin, and Ostlund found that the composition of their mixtures, as determined by absorption at 11.12 μ, varied from one preparation to another. It seems reasonable that the preponderance of chloro compound in one instance and of bromo compound in our mixture may be accounted for by a difference in the ratio of ethyl bromide to amine or in other reaction conditions.

JAMES F. KERWIN
Smith, Kline & French Laboratories
Philadelphia, Pennsylvania

The National Science Foundation and the Scientific Manpower Problem

THE National Science Foundation has now passed into its second year of organized activity. Already its planning and functional accomplishments are evincing trends that are significant of its future course. What is this course in theory and in practice? Does it give promise of achieving its principal goal, which is the broadest possible development of the nation's scientific potential through the critical years ahead?

The foundation's early actions give rise to great hopes for its future—as an agency through which this scientific potential can be directed toward effective ends. Its early grants for basic research have been distributed over the nation on a more equitable population basis than has been the case with any other public or private granting agency. Its first year's fellowship awards show an active and intelligent effort to encourage development in scientifically backward areas of the nation. Certain distributional dangers and pitfalls need sharp re-emphasis, however, if the foundation's efforts are to result in maximal scientific progress in all areas of the nation.

Previous articles (*1, 2*) have dealt with the pitfalls of past distributional techniques, in which current research potential was given much more weight than the longer-term development of the nation's scientific manpower and research possibilities. Funds granted for research will naturally bring greatest immediate results when put to work in institutions best equipped in physical facilities and trained manpower to attack particular scientific problems. Even here there is dependence upon the second and larger aspect of the scientific problem, however, for those institutions best equipped to pursue basic research are already encountering a critical shortage of scientific manpower. All along the line—in industry, educational institutions, and elsewhere—this shortage is becoming steadily more acute.

It is now quite generally agreed that our best efforts must be focused upon the manpower problem and upon its maximal development in all areas of the nation and in all sections of the population. At best, only a small percentage of the total population will be inclined toward a scientific career and especially gifted individuals are as likely to exist in backward areas as in the most progressive. In order that latent talents be discovered early in life, it is necessary that exposure to science be widespread and adequate. Encouragement in the form of fellowships and other grants must be available, but this phase of assistance can come into play only after the gifted individual's interest in science has already been aroused.

The basic attack must thus stem from a broadened exposure (from high schools upward) to *living* science, which can be taught and demonstrated only by those teachers who have had intimate contact with—or participated in—research. Science lives and stimulates interest through research, which thus acquires unique importance to the nation.

Let us, then, analyze the NSF research grants and fellowship awards to June 30, 1952, to see how well it is accomplishing its stated objectives and whether it is falling into past distributional pitfalls. Since the Public Health Service has been the largest granting agency in recent years and has published a comprehensive review (*3*) of research grants by public and private agencies broken down on a geographic basis, we shall use its division of continental USA into seven major areas:

New England: Maine, Vermont, New Hampshire, Massachusetts, Rhode Island, and Connecticut
Middle East: New York, New Jersey, Pennsylvania, Maryland, Delaware, District of Columbia, and West Virginia
Southeast: Virginia, North Carolina, South Carolina, Georgia, Florida, Alabama, Mississippi, Louisiana, Arkansas, Tennessee, and Kentucky
Southwest: Texas, Oklahoma, Arizona, and New Mexico
Central: Ohio, Indiana, Illinois, Michigan, Wisconsin, Minnesota, Iowa, and Missouri
Northwest: North Dakota, South Dakota, Nebraska, Kansas, Colorado, Wyoming, Montana, Idaho, and Utah
Far West: Washington, Oregon, California, and Nevada

Table 1 shows all NSF research and fellowship grants to June 30, 1952, classified on a regional basis. This breakdown does not include applications from, or grants to, those residing or attending colleges outside the continental United States. Two research grants to the National Academy of Sciences could not be classified by region of use and are not included.

Certain significant facts stand out sharply. The scientifically backward Southeast and Southwest are still faring most poorly under the NSF program, whereas the Northwest shows signs of stimulation (more fellowship applications and greater research

TABLE 1

GEOGRAPHIC DISTRIBUTION OF NSF RESEARCH GRANTS AND FELLOWSHIPS
(Per million population, continental USA only)

	Population (1950)						
	New England	Middle East	South-east	South-west	Central	North-west	Far West
	9,314,453	35,632,349	31,783,727	11,375,319	39,957,577	7,883,055	14,647,510
Fellowship applications	26.41 (246)*	26.58 (947)	11.00 (321)	12.66 (144)	18.87 (754)	22.96 (181)	24.10 (353)
Percentage granted	23.1	23.3	16.8	16.7	21.1	16.0	21.2
Fellowships granted							
By home address	6.55 (61)	6.22 (221)	1.70 (54)	2.11 (24)	3.98 (159)	3.68 (29)	5.12 (75)
By college being attended	12.78 (119)	4.04 (144)	1.10 (35)	0.79 (9)	5.36 (212)	1.40 (11)	5.74 (84)
By college to be attended	15.03 (140)	3.67 (131)	0.79 (25)	0.52 (6)	4.75 (190)	0.76 (6)	6.42 (94)
Research funds granted	$99,800	$193,160	$119,950	$52,800	$306,305	$90,300	$173,200
Dollars/million population	$10,715	$ 5,421	$ 3,774	$ 4,642	$ 7,666	$11,455	$ 11,825

* Actual numbers of applications or fellowships granted are indicated in parentheses.

support). These three areas show the smallest percentages of fellowship applications being granted, and this would be expected because of their less well-developed educational facilities in scientific fields. Of more serious portent is the constant drain of young scientists away from these underdeveloped regions, to institutions in the more favored areas. Even the highly industrialized states of the Middle East suffer losses to the better-supported New England institutions. Students leaving the more backward areas for specialized training commonly do not return to permanent residence in their home states, where fewer openings exist for use of their specialized skills. This drain does nothing toward relieving the scientific backwardness of the region and may even accentuate it. This, however, is contrary to the objectives of the NSF as stated in the news release that accompanied the June 30, 1952, announcements of research grants and fellowship awards:

> While grants were selected primarily on the basis of scientific merit, the Foundation is attempting in its research support program to encourage the development of research activities in smaller institutions throughout the United States. This policy not only will increase the research potential of the nation, but it will result in marked improvement in the teaching of Science at both the graduate and undergraduate levels.

In any competitive system of fellowship awards, those sections of the population with an older cultural background and greater density of institutions of higher learning are likely to fare best. In fact, the distributional percentages achieved by the foundation's screening committees indicate that a positive effort must have been made to favor the culturally backward areas, but even stronger efforts should be made in this direction, if the basic purposes of the foundation are to be achieved. Development in the backward areas should be encouraged by their being allotted more than their proportionate share instead of less, even though awards may not always go to those with highest ranking.

Much more disturbing, however, is the fact that 54% of the New England and Middle Eastern sections' fellowship awards were made to students already attending five of the leading educational institutions—Harvard, Yale, Princeton, Columbia, and Massachusetts Institute of Technology; and 71% of the fellowships are to be spent at these same five institutions. Corresponding pecentages elsewhere in the nation are 43% and 54%, and the high-recipient institutions are the universities of Chicago, Illinois, Wisconsin, and California, and California Institute of Technology. Since support of advanced undergraduate or graduate studies in an institution is tantamount to a direct financial grant, this maldistribution of NSF fellowship awards in reality extends greatest help to those students and institutions already making the best progress.

Although the foundation is prohibited by law from dictating where fellowship time shall be spent, it is not prohibited from—but rather is directed toward—taking every possible step to encourage maximal scientific development *in all areas of the nation*. It thus would seem that one primary foundation function should be the encouragement of scientific study in the country's less favored institutions and regions, so as to provide the broadest possible exposure of talented youth to science, even though at present relatively few of the country's institutions of higher learning offer really good facilities for advanced graduate or postgraduate scientific work.

NSF fellowship applications are submitted to three National Research Council screening panels—the Preliminary Predoctoral, the Final Postdoctoral, and the Final Predoctoral. On the Preliminary Predoctoral Screening Panel the New England and Middle Eastern sectors are represented by 12 members (30%), and the remainder of the country by 29 members. On the combined Final Panels, however, these two northeastern sectors have 13 panel members (52%) to 12 for the remainder of the country. Even more significant is the fact that 8 of the 13 are faculty members

of the area's five most favored institutions. The distributional evils arising from such unbalanced screening panel membership have already received adequate consideration (*1*). Is there any possible justification for such unbalanced representation of the large institutions when an ample supply of scientists is available in the country's smaller colleges and universities?

Everything considered, the National Science Foundation does seem to be getting off to a good start. It has achieved a more equitable distribution of its research and fellowship awards than any other granting agency, public or private, up to now. As it settles into more formalized activity through the years, however, it must guard against domination by well-established cultural influences if it would achieve its basic goal—maximal development of scientific manpower in all areas of the nation.

The time may be at hand for transfer to the foundation of many of the National Institutes of Health grants-in-aid activities, perhaps along the lines recently announced by the director of the Biological Sciences Division, Office of Naval Research (*4*).

CLARENCE A. MILLS

Laboratory for Experimental Medicine
University of Cincinnati

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Binucleate Cell Formation in *Melanoplus differentialis* Spermatocytes

THE spermatocyte cysts of the grasshopper testis contain many nuclei, each without a definite cell membrane. The formation of a binucleate cell has been recorded in the course of a time-lapse cinematographic study of cell division, in which Leitz phase-contrast equipment was used.

Spermatocytes in a dextrose-Belar solution in bicarbonate buffer, pH 7.0, were placed on a roto-compressor slide. One of the cells began to divide from a prophase stage, and the metaphase and anaphase stages passed in normal fashion. When early telophase was reached, there was a narrow tubular bridge between the two newly forming daughter cells. The nucleus in each cell developed a nuclear membrane. During the ensuing 6 hr the contracting cell membrane displaced part of the cytoplasm from one daughter cell to the other. In this phase the nuclei remained undisturbed. Finally, at the tubular bridge, between the two daughter cells, a piece of protoplasmic material resembling mitochondria was extruded from the cytoplasm. After this extrusion the narrow bridge began to expand and the cells came together, forming the binucleate cell.

In 1942 Beams and King (*1*) formulated a theory for such binucleate cell formation while they were studying fixed tissue from regenerating rat liver. This work confirms their theory. There may be other types of binucleate cell formation; this is one kind, however, that has been observed and recorded.

T. N. TAHMISIAN

Division of Biological and Medical Research
Argonne National Laboratory, Chicago

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Review of Medical and Veterinary Mycology

SINCE 1944, the Commonwealth Mycological Institute of England has been publishing an annual (now a semiannual) annotated bibliography of the world's literature on medical mycological subjects. The publication, entitled *Review of Medical and Veterinary Mycology*, is very complete in coverage and presents precise summaries of the articles reviewed. We of this laboratory have found the bibliography to be invaluable in keeping informed on developments in this active field of medicine. Undoubtedly, others who are not already acquainted with it will also find this publication to be of value.

It is sold at the nominal charge of 10s. annually. The first number appeared in 1944 (covering the year 1943) under the title *An Annotated Bibliography of Medical Mycology*, and single yearly issues have been published covering the years through 1950. Issues for the years 1943–48 are still available at 6s. each, and the 1949 and 1950 issues at 10s. each. Parts 1 and 2 of the 1951 issue are sold together at 10s.

We are urging those interested to support this publication in order that this service may continue and be utilized by a greater number of workers in medical mycology.

Orders and subscriptions should be placed with The Commonwealth Mycological Institute, Kew, Surrey, England.

LIBERO AJELLO*
LUCILLE K. GEORG
MORRIS A. GORDON

Mycology Unit, U. S. Public Health Service
Communicable Disease Center
Atlanta, Georgia

* The opinions expressed are those of the writers, and do not necessarily constitute endorsement by the U. S. Public Health Service.

Book Reviews

Advances in Medicine and Surgery from The Graduate School of Medicine of the University of Pennsylvania. Philadelphia–London: Saunders, 1952. 441 pp. Illus. $8.00.

This is a well-bound volume well printed on excellent paper. Illustrations, where utilized, are good. The subject matter consists of 52 separate papers designed to cover 10 general subjects. The authorship is multiple and comprises 55 contributors, most of whom are connected with the University of Pennsylvania; a few are guest lecturers.

The purpose of the compilation is to fulfill one of the objectives of the faculty of the University of Pennsylvania Graduate School of Medicine; namely, to publish in book form the symposia given in a postgraduate course for practicing physicians. The subject matter covered is wide and ranges from a consideration of adrenal cortical hormones on through potassium metabolism, thrombo-embolism, cancer, and functional disorders, to mention a few. There is no direct relationship, other than an occasional coincidental one, between the various general subjects.

It goes without saying that no single person is competent to review adequately such a diverse compilation, even if space restrictions did not automatically preclude such an effort. Least of all should a surgeon take on such an assignment if he has any regard for the customary scientific amenities and enough brains to keep out of trouble. Obviously, the reviewer possesses neither.

It is our impression that the editors and authors have done a difficult task well. As is to be expected in any such assembling of material by so many authors, there is considerable variation in the amount of effort expended and in the method and type of subject management. This concerns the length of discussion and clarity of presentation, as well as fidelity, authenticity, and style of narration. Probably the most serious and most inexcusable breach of fidelity was encountered in Henle's article on mumps, wherein he fails completely to mention the obvious pertinence and priority of Goodpasture's outstanding, classical work. This is the bedrock on which Henle's article rests but, oddly, he inferentially (p. 384, line 3) ascribes it to others.

The reviewer has been interested for years in the efforts of some members of the preclinical medical faculties to stray over into the clinical aspects of medicine. By and large, it is our impression that they do it less gracefully, perhaps with less deftness, than the clinicians, who in turn are poaching along the fringes of pure science.

This volume interestingly illustrates the foregoing without detracting from its charm or real intrinsic value. Each general section is well and interestingly done. To do justice to each of the numerous contributors would require individual mention of each. Limitation of space makes this impractical, although the volume warrants such treatment. In our estimation, this compilation may be read with interest and profit by any physician, irrespective of his field of special interest. Therefore, it is sincerely recommended.

KARL H. MARTZLOFF

Department of Surgery
University of Oregon Medical School

Biochemistry and Human Metabolism. Burnham S. Walker, William C. Boyd, and Isaac Asimov. Baltimore: Williams & Wilkins, 1952. 812 pp. Illus. $9.00.

Some of the textbooks in biochemistry published during the past 15 years have, by the introduction of a few clinical applications, emphasized the interests of medical students. Others, written expressly for medical students, have not adequately combined the fundamentals of the subject with the medical viewpoint. As in other sciences, the authors of textbooks in biochemistry are faced with two difficult problems. The first is that of inclusion or exclusion of material. The border lines between biochemistry, physiology, pharmacology, and microbiology have never been very clear and are becoming less so as these fields develop. The second is that of arrangement of the material for maximum teaching effectiveness. Although the answer to this problem may lie in part in pedagogical theory, the solution usually grows out of the personal ideas and experience of the authors.

Biochemistry and Human Metabolism is intended primarily for medical students. The classical order of topics has been altered extensively. Part I, comprising four chapters, is entitled "Structure." "The Chemistry of Proteins" (Chaps. 1 and 2) is taken up first because of the authors' opinion that these substances are of prime importance to medical biochemistry. "The Chemistry of Carbohydrates and Lipids" is presented as an introduction to tissue chemistry (Chap. 3 of Part I). The fourth chapter deals with blood and the anemias. Part II, designated "Control," contains the usual material on enzymes and hormones. In Part III, "Growth," there are chapters on nucleoproteins, cancer, and reproduction and heredity. Part IV, "Metabolism," takes up food and diet, digestion, intermediary metabolism, electrolytes and water, respiration, heat and work, and excretion. "Vitamins and Vitamin Deficiency Diseases," and "Infection" make up Part V, "Pathology." Colloids, isotopes, thermodynamics, and acids and bases are covered in the appendix.

The success of a textbook as a tool in the teaching process is difficult to forecast. It seems evident, however, that a mere reshuffling of topics does not in itself constitute a real improvement. Moreover, it leads to certain teaching difficulties, such as the postponing of basic definitions and concepts until after their application and significance have been discussed. There is

still much to be said for the classical arrangement of proceeding from the simple to the complex; from the known to the unknown. Many instructors in medical biochemistry cover the material included in the appendix of the present volume in the early part of their courses.

The chapter on "Reproduction and Heredity" contains a 30-page section on genetics and blood groups. The necessity of including this and a 23-page chapter on cancer in a textbook of medical biochemistry may be questioned, especially when "Lipid Metabolism and Ketosis" is covered in 12 pages, and "Proteins and Starvation" in 27.

In general, the authors have been successful in integrating the basic and clinical aspects of the subject. The clinical applications are well chosen and of current interest. The volume should be especially valuable to physicians and interns who wish to review recent advances on the subject. Assessment of its value as a text for students beginning the study of biochemistry must await the test of usage.

CARLETON R. TREADWELL
Department of Biochemistry
George Washington University Medical School

Problems in Physical Chemistry. English ed. Lars Gunnar Sillén, Paul W. Lange, and Carl O. Gabrielson. New York: Prentice-Hall, 1952. 370 pp. $5.50.

For some time this reviewer has felt the need for a problem source book as an aid in teaching physical chemistry. To a very large extent this need is satisfied by the translation of Sillén, Lange, and Gabrielson's Swedish text, which contains more than 700 problems, with answers, covering "classical" physical chemistry—e.g., 100 problems relating to thermodynamics, 75 to electrochemistry, 75 to chemical kinetics. The problems in each set are graduated as to difficulty, and, in most cases, reference is given to the original literature.

It is unfortunate that contrary to American usage the work done by a thermodynamic system is defined to be negative and, thus, the first law is written $\Delta E = q + W$. However, since this convention, and all others, are very clearly stated in the text, this change in sign should cause only momentary confusion in the mind of the reader. It is felt that the inclusion of problem sets relating to nuclear chemistry, atomic and molecular structure, and the more elementary concepts of quantum mechanics would have greatly enhanced the usefulness of the book when used in conjunction with a modern textbook such as Moore's.

Although of minor importance, it is very pleasing to see the book begin on page 1 with the generalized mol concept and ignore completely the superfluous terms gram-atom, gram-ion, etc.

Sillén's manual clearly can be useful to the lecturer, but its adoption for student use may be problematical. The discussion accompanying each problem set is exceptionally lucid, but necessarily concise; therefore, it seems doubtful that the book could stand alone as a text. On the other hand, there may be a reluctance to ask students to purchase this problem book in addition to a conventional textbook. The usefulness of this manual to the student, however, may well outweigh the monetary consideration.

The authors begin the introduction with the statement: "The student who would learn to solve physicochemical problems with confidence must be prepared for a fair amount of mental effort." The reader who works his way through the book will also have used "a fair amount of mental effort" but will be more than amply repaid for his labor.

M. KENT WILSON
Department of Chemistry, Harvard University

The Stars: A New Way to See Them. H. A. Rey. Boston: Houghton Mifflin, 1952. 143 pp. Illus. $4.00.
Pictorial Astronomy. Dinsmore Alter and Clarence H. Cleminshaw. New York: Crowell, 1952. 296 pp. Illus. $4.50.

There are unfortunately many authors who must "talk down" to their readers because they have no confidence in the earnestness and intelligence of the ordinary fellow. These authors are usually amateurs in the fields in which they write. Others, who are professionals, have learned the knack of writing lucidly, yet informatively and authoritatively. In these books we have examples of these two contrasting types.

The jacket blurb for the book by Rey speaks of the author as having "swept out the meaningless and confusing geometrical shapes that have baffled the beginning star-gazer for centuries." To justify this statement, there are pages of contrasting "old" and "new" representations, but few will recognize the "old" ones as authentic. In many instances the author has drawn absurd "old" diagrams which he has then contrasted with "new" ones that many of us have been using right along. When he does do a really new one, such as for Ursa Major or for Pegasus, he often corrupts the traditional descriptions and reverses the figures, doing a far worse job than has been done in the past.

I know from my own experience that in several planetarium cities the "new" figures of Rey have been used for many years, and some others that are far superior to his. Not all the figures are bad; many of them are good "old" ones. The jacket itself, when unfolded, is a very useful map of the Northern sky. The text and illustrations in the second half of the book, devoted to general information in astronomy, are rather good. Certainly, some new stargazers will be attracted by this book—always a good thing.

The second book is written by two professionals who have devoted many years to extending public knowledge and appreciation of astronomy at the Griffith Planetarium in Los Angeles. There are 10 pages of star maps of various kinds, but most of the 56 chapters are devoted to very lucid discussions of specific topics in astronomy, intended for the average interested but uninformed person, even some rather young ones.

Alter and Cleminshaw have had millions of people

in their lectures, and they have tried out the material of this book in the monthly magazine published at their institution. The great number of illustrations includes diagrams and sketches, as well as fine photographs, well reproduced. Not as fresh-looking as Rey's book, this one has perhaps twenty times as much information in it, while requiring about twice the concentration to dig it out. When dug, however, it is sound.

ROY K. MARSHALL
2017 Haverford Road, Ardmore, Pennsylvania

Soil Physical Conditions and Plant Growth. Vol. II of *Agronomy*. Byron T. Shaw, Ed. New York: Academic Press. 1952. 491 pp. $8.80.

This book, prepared under the auspices of the American Society of Agronomy, is a compilation by nine authors of five principal divisions dealing with the effect of the physical condition of the soil upon plant growth. The introduction by the editor succinctly states the purpose of the book:

> It is the purpose of this monograph to provide students and professional agriculturists with a critical and authoritative evaluation of the present knowledge on this subject and to point out those areas in which additional data are needed.
>
> It is postulated that all physical attributes of the soil, such as apparent density, aggregation, pore-size distribution, friability, and others, influence plant growth through their effects on: (1) soil moisture, (2) soil air, (3) soil temperature, and (4) mechanical impedance to root development and shoot emergence. The first chapter of the monograph describes the soil as a physical system and considers methods by which the physical characteristics of the soil can be modified. The succeeding chapters deal with each of the four fundamental edaphic factors previously listed. In each chapter a description of the essential features of the phenomenon is first given. This is followed by a discussion of how the physical character of the soil affects the particular edaphic factor being discussed. An evaluation of the significance of that factor to plant growth follows. In the final chapter the interactions among the four fundamental factors are discussed in relation to other factors affecting plant growth.

In addition to consideration of the direct effect of physical properties of the soil on plant growth, indirect effects of these properties upon nutrient supply, pH, etc., are considered.

The five divisions of the book are: "Soil as a Physical System," by Lyle T. Alexander and H. E. Middleton; "Mechanical Impedance and Plant Growth," by J. F. Lutz; "Soil Water and Plant Growth," by L. A. Richards and C. H. Wadleigh; "Soil Aeration and Plant Growth," by M. B. Russell; and "Soil Temperature and Plant Growth," by S. J. Richards, R. M. Hagan, and T. M. McCalla. All chapters are thoroughly documented, including the most comprehensive review of the literature on the respective chapters that this reviewer has seen.

This book is of first importance to senior and graduate students in soils, to professional agriculturists, and to botanists engaged in research. In addition, this reviewer feels that the book could be used profitably as a text in soil classes where the application of soil physical properties to plant growth is emphasized.

The authors and editor are to be commended for an outstanding summary of the literature, of great value to all technical workers interested in the growth of plants.

C. B. TANNER
Department of Soils, University of Wisconsin

Scientific Book Register

Improving Undergraduate Instruction in Psychology. Report of a study group supported by the Carnegie Corporation of New York and the Grant Foundation which met at Cornell University, June 27–August 16, 1951. Dael Wolfle, Chairman. New York: Macmillan. 1952. 60 pp. $1.25.

Science and Hypothesis. Repr. H. Poincaré. New York: Dover, 1952. 244 pp. $2.50; $1.25 paper.

Forestry and Its Career Opportunities. Hardy L. Shirley. New York–London: McGraw-Hill, 1952. 492 pp. Illus. $6.50.

Investment Castings for Engineers. Rawson L. Wood and Davidlee Von Ludwig. New York: Reinhold, 1952. 477 pp. Illus. $10.00.

Food and Population and Development of Food Industries in India. Mysore: Central Food Technological Research Institute, 1952. 357 pp. Illus.

Styrene: Its Polymers, Copoloymers and Derivatives. American Chemical Society Monograph 115. Ray H. Boundy and Raymond F. Boyer, Eds. New York: Reinhold, 1952. 1304 pp. Illus. $20.00.

Annual Review of Physical Chemistry, Vol. 3. G. K. Rollefson, Ed., and R. E. Powell, Assoc. Ed. Stanford, Calif.: Annual Reviews, 1952. 416 pp. Illus. $6.00.

The Immaculate Forest. An account of an expedition to unexplored territories between the Andes and the Amazon. W. R. Philipson. New York: Philosophical Library, 1952. 223 pp. Illus. $4.50.

Semimicro Qualitative Analysis. 3rd ed. Paul Arthur and Otto M. Smith. New York–London: McGraw-Hill, 1952. 285 pp. Illus. $4.00.

Polarography: Inorganic Polarography, Organic Polarography, Biological Applications, Amperometric Titrations, Vol. II. 2nd ed. I. M. Kolthoff and James J. Lingane. New York–London: Interscience, 1952. 990 pp. Illus. $11.00.

Contributions to the Theory of Nonlinear Oscillations, Vol. II. S. Lefschetz, Ed. Princeton, N. J.: Princeton Univ. Press, 1952. 116 pp. $1.50.

The Evolution of Chemistry: A History of Its Ideas, Methods, and Materials. Eduard Farber. New York: Ronald Press, 1952. 349 pp. Illus. $6.00.

Fundamentals of Engineering Electronics. 2nd ed. William G. Dow. New York: Wiley; London: Chapman & Hall, 1952. 627 pp. Illus. $8.50.

Nerve Impulse. Transactions of the Third Conference, March 3–4, 1952, New York. H. Houston Merritt, Ed. New York: Josiah Macy, Jr. Fdn., 1952. 176 pp. Illus. $3.50.

Theory of Numbers. B. M. Stewart. New York: Macmillan, 1952. 261 pp. Illus. $5.50.

Organic Syntheses, Vol. 32. Richard T. Arnold, Ed. New York: Wiley; London: Chapman & Hall, 1952. 119 pp. $3.50.

Publications Received

Age Is No Barrier. Albany: New York State Joint Legislative Committee on Problems of the Aging, 1952. 171 pp. Illus. Free.

The Commercial Fish Catch of California for the Year 1950 with a Description of Methods Used in Collecting and Compiling the Statistics. Fish Bull. No. 86. Staff, Bureau of Marine Fisheries. 120 pp. Illus. ***Surveys Through 1951 of the Distribution and Abundance of Young Sardines*** Sardinops caerulea. Fish Bull. No. 87. Julius B. Phillips and John Radovich. 63 pp. Illus. State of California, Dept. Fish and Game, Bur. of Marine Fisheries, 1952.

Committee on Growth of the National Research Council, Sixth Annual Report to American Cancer Society, Inc., July 1950–June 1951. Washington, D. C.: Division of Medical Sciences, National Research Council. 373 pp. Free.

The Common and Systematic Nomenclature of the Simpler Organic Compounds. Fred Semeniuk. School of Pharmacy, University of North Carolina. Chapel Hill, N. C. Pharmaceutical Research Foundation, 1952. 55 pp. $1.25.

Conference on the Mechanisms of Hormone Action with Special Reference to the Adrenal Cortical Hormones, Pub. 224. Washington, D. C.: National Academy of Sciences–National Research Council, 1952. 15 pp. Free.

Cortone, A Handbook of Therapy. Rahway, N. J.: Merck & Co., 1952. 129 pp. Free to physicians and pharmacists.

Cyclopygid Trilobites from Girvan and a Note on Bohemilla, Vol. 1, No. 10. W. F. Whittard. London: British Museum (Natural History), *Geology,* 1952. Pp. 307–21 + 2 plates. 6s.

Dextran—A Selected Bibliography. Chemical, Microbiological, Clinical, and Related Publications of Interest in the Use of Dextran as a Synthetic Blood Volume Expander. Allene Jeanes. Peoria, Ill.: USDA, Northern Regional Research Laboratory, 1952. 42 pp. Free.

Eastman Organic Chemicals, List No. 38. Rochester, N. Y.: Distillation Products Industries, 1952. 224 pp. Free.

Ecological Crop Geography and Field Practices of the Ryukyu Islands, Natural Vegetation of the Ryukyus, and Agro-Climatic Analogues in the Northern Hemisphere. M. Y. Nuttonson. Washington, D. C.: Am. Inst. Crop Ecology, 1952. 106 pp. Illus. $3.00.

Geophysical Research Papers: Atmospheric Flow Patterns and Their Representation by Spherical-Surface Harmonics. No. 14. July 1952. B. Haurwitz and Richard A. Craig. 78 pp. Illus. ***Back Scattering of Electromagnetic Waves from Spheres and Spherical Shells.*** No. 15. July 1952. A. L. Aden. 42 pp. Illus. ***Notes on the Theory of Large-Scale Disturbances in Atmospheric Flow with Applications to Numerical Weather Prediction.*** No. 16. July 1952. Philip Duncan Thompson. 106 pp. ***The Observed Mean Field of Motion of the Atmosphere.*** No. 17. August 1952. Yale Mintz and Gordon Dean. 65 pp. Illus. Cambridge, Mass.: Geophysics Research Division, Air Force Cambridge Research Center, Air Research and Development Command.

Graphic Regional Sociology. Carle C. Zimmerman and Richard E. Du Wors. Cambridge, Mass.: Phillips Book Store, 1952. x + 206 pp. Illus. $3.50.

Meetings & Conferences

Dec. 1–6. National Exposition of Power and Mechanical Engineering. Grand Central Palace, New York.

Dec. 3–4. Animal Care Panel (Annual). University of Illinois, Chicago.

Dec. 4. Society of Cosmetic Chemists (Annual). Biltmore Hotel, New York.

Dec. 6–9. American Academy of Optometry (Annual). Hotel Seneca, Rochester, N. Y.

Dec. 7–10. American Institute of Chemical Engineers (Annual). Hotel Cleveland and Carter Hotel, Cleveland.

Dec. 12–13. Association for Research in Nervous and Mental Disease (Annual). Hotel Roosevelt, New York.

Dec. 13–16. American Institute of Chemical Engineers (Annual). St. Louis.

Dec. 23–27. Symposium on Scientific Principles and their Application in Tropical Building Design and Construction. New Delhi, India.

Dec. 26–30. American Physical Society. Naval Ordnance Test Station, Inyokern, and California Institute of Technology, Pasadena, Calif.

Dec. 26–31. American Association for the Advancement of Science (Annual). Hotel Jefferson, St. Louis.

Dec. 27–28. American Chemical Society. Division of Industrial and Engineering Chemistry (Annual Chemical Engineering Symposium). Evanston, Ill.

Dec. 27–29. American Mathematical Society (Annual). Washington University, St. Louis.

Dec. 27–Jan. 3. Basic Seminar in General Semantics. Institute of General Semantics, Lakeville, Conn.

Dec. 28. International Union Against Cancer and International Cancer Research Commission. Bombay.

Dec. 28–29. Committee for the Scientific Study of Religion. New York.

Dec. 30. Mathematical Association of America, Inc. Washington University, St. Louis.

Jan. 9–10. American Group Psychotherapy Association (Annual). Henry Hudson Hotel, New York.

Jan. 12–16. Society of Automotive Engineers (Annual). Sheraton-Cadillac Hotel, Detroit.

Jan. 13–16. Highway Research Board (Annual). National Academy of Sciences–National Research Council, Washington, D. C.

Jan. 14–16. Conference on High-Frequency Measurements, sponsored by American Institute of Electrical Engineers, Institute of Radio Engineers, and the National Bureau of Standards. NBS, Washington, D. C.

Jan. 19–23. American Institute of Electrical Engineers (Winter General). Hotel Statler, New York.

Jan. 20–31. Inter-American Congress of Philosophy. Havana.

Jan. 22–24. American Physical Society (Annual). Harvard University, Cambridge, Mass.

Jan. 26–27. Compressed Gas Association, Inc. (Annual). Waldorf-Astoria Hotel, New York.

Jan. 26–29. American Society of Heating and Ventilating Engineers (Annual). Conrad Hilton Hotel, Chicago.

Jan. 26–30. International Heating and Ventilating Exposition. International Amphitheatre, Chicago.

Jan. 30. Public Health Workshop, First District Dental Society of the State of New York. Hotel Statler, New York.

Jan. 30–31. Western Society for Clinical Research (Annual). Carmel, Calif.

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